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CLINICAL USE OF BLOOD DERIVATIVES

CHARLES A. JANEWAY, M.D.
Boston

Physiologic reasoning underlies sound practice in all fields of medicine today. But physiology, in turn, is dependent on chemistry for insight into the fundamental nature of the phenomena of health and disease. The work of a distinguished company of clinicians and medical scientists over a long period of years has evolved our present state of knowledge of the multiple functions of the blood and of their dependence on the molecular properties of the specific proteins by which they are mediated.

The development of blood derivatives stems logically from this concept that each function of the blood is due to one or more specific components. Great progress has been made in the decade since plasma first came into general clinical use as a derivative of blood in which its osmotic and certain of its nutritional properties could be preserved for use when separated from the more labile cells. Chemical and physical advances have led to better preservation of the cellular components and to the introduction of large scale methods for the separation and purification of plasma proteins for clinical use. These developments not only have yielded important therapeutic results but have given investigators new tools with which to obtain a more thorough understanding of human physiology and its derangements in disease. For example, a β_1-globulin, which has been crystallized from fraction IV-*7* of human plasma,[2] accounts for the capacity of the plasma to bind and transport iron.[3] Isolated in pure form, it has been possible to study the reactions of this protein with iron in the laboratory and to make parallel observations on patients.[4] From these investigations has come new insight into iron metabolism and transport, although no disease has yet been found in which a deficiency of this metal-binding globulin requires replacement.

In discussing the clinical use of blood derivatives, it is important to reemphasize the difference between stimulation and replacement therapy. In the former, the patient is stimulated to replenish his own deficit (e. g., the treatment of hypochromic anemia with iron salts) while in the latter, the deficiency is made up by passive transfer from a donor. This has the advantage of immediate rectification of the deficiency, but the effect is relatively short lived and does not reach the fundamental cause. Blood derivatives are indicated for the replacement therapy of specific deficiencies of the blood, whenever speed is important or stimulation therapy is not effective or not available.

Figure 1 clearly indicates the gross differences in composition between certain available derivatives, and the reason that their use for specific indications leads to greater therapeutic effectiveness. Since the recruitment of donors is the most difficult practical task in any blood program, the economy in the use of blood made possible by its separation into fractions, in each of which one or another specific function is concentrated, is of considerable importance. The extent to which the usefulness of a single donation of blood can be magnified by fractionation is seldom appreciated. Table 1 shows what can be derived from the fractionation of twenty blood donations. A glance at the column marked "Dating Period" brings out another important consideration. Many of the important blood components are labile and undergo rapid deterioration in whole blood. Separated and concentrated, each may be packaged in a state best adapted to the preservation of its functional activity, ready for clinical use whenever and wherever it is needed.

BLOOD CELLS

The cellular components of the blood deserve further chemical study. Satisfactory methods for concentration and preservation of the unstable granulocytes and platelets do not exist. Because the red cells contain the most important blood protein, hemoglobin, which is responsible for the vital function of oxygen transport, considerable effort has been expended in improving methods for their preservation. At present, cells taken

From the Department of Pediatrics, Harvard Medical School and the Children's Medical Center, Boston.

Read in the General Scientific Meetings at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 22, 1948.

This paper is number 74 in the series "Studies on the Plasma Proteins" from the Harvard Medical School, Boston, on products developed by the Department of Physical Chemistry from blood collected by the American Red Cross.

This work was originally supported by grants from the Rockefeller Foundation and from funds of Harvard University. It was aided early in 1941 by grants from the Committee on Medicine of the National Research Council, which included a grant from the American College of Physicians. From August 1941 to July 1946, it was carried out under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University. Since then it has been aided by a grant, recommended by the Panel of Hematology of the National Institute of Health, from the United States Public Health Service.

1. Footnote deleted in proof.

2. Koechlin, B. A.: Crystallization and Characteristics of a Metal Binding β_1-Pseudoglobulin from Human Plasma, to be published.

3. Schade, A. L., and Caroline, L.: Iron-Binding Component in Human Blood Plasma, Science **104**: 340, 1946. Surgenor, D. M.; Koechlin, B. A., and Strong, L. E.: The Metal Combining Globulin of Human Plasma: XXXVII. Chemical, Clinical and Immunobiological Studies of the Products of Human Plasma Fractionation, J. Clin. Investigation, to be published.

4. Rath, C. E., and Finch, C. A.: Measurement of Iron Binding Capacity of Serum in Man: XXXVIII. Serum Iron Transport, J. Clin. Investigation, to be published. Cartwright, G. D.; Black, P., and Wintrobe, M. M.: Studies on the Iron Binding Capacity of Serum: XXXIX. The Anemia of Infection, J. Clin. Investigation, to be published.

into chilled bottles containing some modification of the ACD formula and allowed to sediment at 4 C. will keep about as well with most of the plasma removed as they would if kept as whole blood.[5] The amounts of hemoglobin relative to plasma protein and sodium in whole blood and in red cell suspensions shown in figure 1 apply to the Children's Medical Center, where a modified ACD solution, 70 cc. to 500 cc. of blood, is used. After sedimenting in the cold overnight and withdrawal of the supernatant plasma, the cells may be resuspended by shaking, and the suspension, which has a hematocrit reading of approximately 65 per cent, can be used without dilution.[6] Cell suspensions require filtration through gauze or wire mesh and must be mixed with slightly hypertonic sodium chloride solution (1 per cent) if a diluent is used. Red cell suspensions have two great advantages in the treatment of patients with anemia of all types except those due to acute blood loss or severe infection, where there may be a deficit of plasma protein as well. First, they supply more hemoglobin with less of the osmotic activity of the plasma proteins and with less sodium, thus increasing the dose that can be safely given without overloading the circulation. Second, while they provide material for replacement of hemoglobin deficits, the plasma which the patient does not need is saved for other uses. The effectiveness of red cell suspensions was clearly demonstrated[7] even before the substitution, for sodium citrate solution in which 70 per cent of the cells remain viable for only seven to ten days, of ACD solution in which 70 per cent viability can be extended to at least twenty-one days.[8] An important consideration in the use of cell suspensions is the demonstration by the radioactive-iron technic that the iron of the nonviable cells can be efficiently reutilized for hemoglobin synthesis.[9] More work needs to be done in extending the period of life of the red cell in vitro and in the development of practical methods for the general distribution and clinical use of red cell suspensions.

TABLE 1.—*Effect of Fractionation on Utilization of Twenty Blood Donations*

Derivative	Dating Period	Clinical Use	No. Packages	No. Patients Treated	Total
Whole blood.....	21 days	Hemorrhage	20	20	20
		Separation of Cells and Plasma			
Red cells.....	21 days	Anemia	20	20	30
Dried plasma.....	5 yr.	Shock, hypoproteinemia	10	10	
		Fractionation of Blood			
Red cells.....	21 days	Anemia	20	20	135
Fraction I.....	1 yr.	Hemophilia, surgery	30*	30	
Gamma globulin.....	3 yr.	Prophylaxis of infections	80	80	
Serum albumin.....	5 yr.	Shock, hypoproteinemia	5	5	
Isohemagglutinins†..	1 yr.	Blood grouping	100	2,000	2,150
Thrombin †.....	1 yr.	Hemostasis	150	150	
Other fractions.....	.....	Further research	...	...	...

* Alternatives: fibrin foam or fibrin film.

† Yield of these products is so large that they need be produced only from occasional runs.

The processes of chemical fractionation have been applied to the red cell as well as to the plasma. Methods for the preparation of hemoglobin in a relatively stable state have led to investigations of its physiologic activity in solution.[10] Hemoglobin solutions combine oxygen-carrying power with high osmotic activity (the molecular weight of hemoglobin is about the same as that of serum albumin, although it can split into two half-molecules) and therefore act dramatically in experimental shock. Although a few preliminary studies on the use of hemoglobin in shock in human beings have been made, the fact that renal function is temporarily depressed when it is given to experimental animals has properly made all investigators cautious about its clinical use.[11] It is not by accident that nature has chosen to surround hemoglobin at a concentration of 30 per cent with the semipermeable membrane of the erythrocyte. A derivative of hemoglobin, modified globin, has been developed to act as a plasma protein substitute.[12] Further work will be needed before its place in therapy can be finally evaluated. Globin offers the possibility of salvaging the large amount of protein in outdated red cells for nutritional use. The considerable number of active enzymes—catalase, hypertensinase, choline esterase and others—found in the erythrocyte should stimulate further work on their purification from this important human source.

PLASMA

The value of plasma as an emergency blood substitute in the treatment of shock due to blood loss is too well known for further comment. As Evans has indicated, plasma and albumin are substitutes for blood, providing colloid osmotic activity, salts and water which will replace the blood lost and restore the circulation, but lacking the oxygen carrying power of hemoglobin. Thus the plasma-treated or albumin-treated shock patient may recover from his shock, but will then be an anemic patient,[13] with tachycardia, diminished tolerance to exercise and possibly a slower rate of healing. However, the most serious difficulty with plasma has arisen from the practice of pooling and from the excel-

5. Gibson, J. G., II; Evans, R. D.; Aub, J. C.; Sack, T., and Peacock, W. C.: The Post-Transfusion Survival of Preserved Human Erythrocytes Stored as Whole Blood, or in Resuspension, After Removal of Plasma, by Means of Two Isotopes of Radioactive Iron, J. Clin. Investigation **26**: 715-738, 1947.

6. Flynn, F.: Personal communication to the author.

7. Taylor, E. S.; Thalhimer, W., and Cooksey, W. B.: The Organization of a Red Blood Cell Transfusion Service, J. A. M. A. **124**: 958-690 (April 1) 1944. Cooksey, W. B., and Horwitz, W. H.: The Use of Salvaged Red Cells, ibid. **124**: 961-964, 1944.

8. Rapoport, S.: Dimensional, Osmotic, and Chemical Changes of Erythrocytes in Stored Blood: I. Blood Preserved in Sodium Citrate, Neutral and Acid-Citrate-Glucose (ACD) Mixtures, J. Clin. Investigation **26**: 591-615, 1947; II. Evaluation of Several Acid and Neutral Preservation Mixtures, ibid. **26**: 616-621, 1947; III. Comparison of Three Dilutions of Acid Citrate-Glucose Solution (ACD), ibid. **26**: 622-628, 1947. Strumia, M. M.; Blake, A. D., and Wicks, W. A.: The Preservation of Whole Blood, ibid. **26**: 667-671, 1947. Strumia, M. M.; Blake, A. D., and McGraw, J. J., Jr.: An Acid Citrate-Dextrose Solution with Low Water Volume and Low Dextrose Concentration, ibid. **26**: 678-686, 1947. Ross, J. F.; Finch, C. A.; Peacock, W. C., and Sammons, M. E.: The in Vitro Preservation and Post-Transfusion Survival of Stored Blood, ibid. **26**: 687-703, 1947.

9. Gibson, J. G., II; Peacock, W. C.; Evans, R. D.; Sack, T., and Aub, J. C.: The Rate of Post-Transfusion Loss of Non-Viable Stored Human Erythrocytes and the Reutilization of Hemoglobin-Derived Radio-Active Iron, J. Clin. Investigation **26**: 739-746, 1947.

10. Hamilton, P. B.; Farr, L. E.; Hiller, A., and Van Slyke, D. D.: Preparation of Hemoglobin Solutions for Intravenous Infusions, J. Exper. Med. **86**: 455-463, 1947. Farr, L. E.; Hiller, A., and Van Slyke, D. D.: Preparation of Dried Hemoglobin Without Loss of Activity, ibid. **86**: 465-475, 1947.

11. Hamilton, P. B.; Hiller, A., and Van Slyke, D. D.: Renal Effects of Hemoglobin Infusions in Dogs in Hemorrhagic Shock, J. Exper. Med. **86**: 477-487, 1947. Lalich, J. J.: The Influence of Injections of Homologous Hemoglobin on the Kidneys of Normal and Dehydrated Animals, ibid. **86**: 153-158, 1947; The Influence of Available Fluid on the Production of Experimental Hemoglobinuric Nephrosis in Rabbits, ibid. **87**: 157-162, 1948. Rather, L. J.: Renal Athrocytosis and Intracellular Digestion of Intraperitoneally Injected Hemoglobin in Rats, ibid. **87**: 163-173, 1948. Harrison, H. E.; Bunting, H.; Ordway, N. K., and Albrink, W. S.: The Pathogenesis of the Renal Injury Produced in the Dog by Hemoglobin or Methemoglobin, ibid. **86**: 339-356, 1947.

12. Strumia, M. M.; Chornock, F. W.; Blake, A. D., and Karr, W. C.: The Use of "Modified Globin" from Human Erythrocytes as a Plasma Substitute, Am. J. M .Sc. **209**: 436-443, 1945. Strumia, M. M.; Chornock, F. W.; Blake, A. D., and Reider, H. C.: The Use of "Modified Globin" from Human Erythrocytes in Hypoproteinemias, ibid. **211**: 51-62, 1946.

13. Cournand, A.; Noble, R. B.; Breed, E. S.; Lauson, H. D.; Baldwin, E. DeF.; Pinchot, G. B., and Richards, D. W., Jr.: Clinical Use of Concentrated Human Serum Albumin in Shock, and Comparisen with Whole Blood and with Rapid Saline Infusion, J. Clin. Investigation **23**: 491-506, 1944.

lence of the method of drying from the frozen state used to preserve its labile components, both of which, combined with the stability of the virus, have led to the spread of homologous serum jaundice by means of pooled dried plasma. Table 2, which gives the best available statistics, indicates the relationship of the

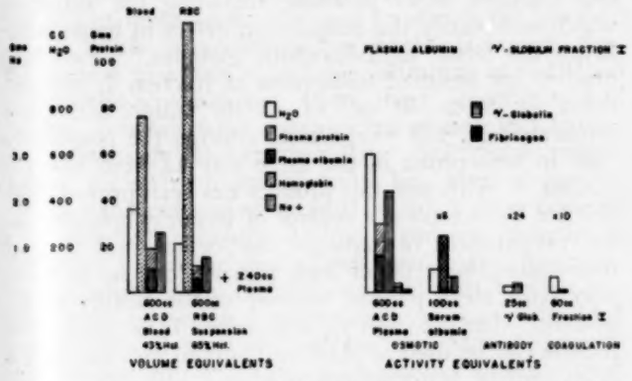

Fig. 1.—Comparison of composition of blood and certain derivatives with respect to water and sodium and their major protein components.

incidence of serum hepatitis to the size of the pool. The statistics for this country have been gathered through studies initiated by the American Red Cross as part of its blood program. Although no cases were observed after blood or single serum transfusions in the series reported, the disease has been recorded in scattered patients who have received only whole blood transfusions.[14] The statistics for the plasma fractionation products are incomplete, but with the very large pools used, the expected incidence would be very high, while in actual fact it has been negligible, except with fraction I.

The control of this disease is one of the most important practical problems in medicine. Three approaches are possible; first, development of better screening methods for infectious donors; second, development of methods of immunization against the disease, and, third, development of methods for the sterilization of blood and plasma. Work on all three lines is in progress, but the third approach seems most promising. Although proof has not yet been obtained that ultraviolet irradiation, which acts by its effect on certain proteins, will inactivate known hepatitis virus in large scale processing without altering the labile proteins chemically, there is sufficient evidence of its effectiveness to be optimistic.[15] Passive immunization with human gamma globulin has yielded equivocal results and hardly seems practicable except for the recipients of a pool found to be infected.[16] At the present time, pooled plasma should be used only for clear indications when neither blood nor serum albumin are available.

14. Beeson, P. B.: Jaundice Occurring One to Four Months After Transfusion of Blood or Plasma, J. A. M. A. **121**: 1332-1334 (April 24) 1943.

15. Oliphant, J. W., and Hollaender, A.: Homologous Serum Jaundice: Experimental Inactivation of Etiologic Agent in Serum by Ultraviolet Irradiation, Pub. Health Rep. **61**: 598-602, 1946. Wolf, A. M.; Mason, J.; Fitzpatrick, W. J.; Schwartz, S. O., and Levinson, S. O.: Ultraviolet Irradiation of Human Plasma to Control Homologous Serum Jaundice, J. A. M. A. **135**: 476-477 (Oct. 25) 1947. Blanchard, M. C.; Stokes, J., Jr.; Hampil, B.; Wade, G. R., and Spizizen, J.: II. The Inactivation of Hepatitis Virus SH (Homologous Serum Hepatitis) by Ultraviolet Irradiation, ibid. **138**: 341-343, 1948.

16. Grossman, E. B.; Stewart, S. G., and Stokes, J., Jr.: Post-Transfusion Hepatitis in Battle Casualties and Study of Its Prophylaxis by Means of Human Immune Serum Globulin, J. A. M. A. **129**: 991-994 (Dec. 8) 1945. Blanchard, M., Jr.; Stokes, J., Jr.; Neefe, J. R.; Gellis, S. S., and Wade, G. R., Jr.: I. Studies in the Protective Value of Gamma Globulin in Homologous Serum Hepatitis SH Virus, ibid., **138**: 336-341, 1948.

PLASMA FRACTIONS

The development of large scale methods for the concentration of the protein components of human plasma into fractions, from which various derivatives can be prepared in the form best adapted to preserve their physiologic activity for therapeutic use, has had an important impact on many phases of medicine.[17] These methods, designed for the separation of specific proteins from mixtures, have been applied to the purification of virus vaccines, toxoids, animal serums and tissue extracts, as well as plasma. Although introduced for the separation of half of the plasma protein, serum albumin, from the remaining less stable globulins, so as to provide a compact stable blood substitute during the war, the methods are inclusive, so that a single fractionation process yields all the major components of plasma with minimal losses and minimal denaturation of the labile components. During the Army-Navy-Red Cross blood program of the war, slightly more than two million blood donations were subjected to fractionation, yielding products which were used by the armed forces, returned to the American people when surplus and used in part for research. Since the war, the Red Cross has continued the distribution of surplus blood derivatives—plasma and the products of plasma fractionation—for therapeutic use when the supply has been adequate and the value proved, or for clinical investigation in other instances. Small amounts are also available from one commercial source. The following brief résumé of the present status of the plasma fractionation products is based on published data, personal experience and the work of

TABLE 2.—*Homologous Serum Jaundice*

Derivative	Maximum No. Donors per Lot	No. Recipients	Incidence, Percentage
Whole blood	1	891 *	0
		750 †	0 ‡§
		821 ‖ (children)	0
Single serum	1	573 ¶	0
Pooled plasma or serum	400	1,054 *	7.3
Pooled dried plasma	50	649 #	4.5
		1,200 †	3 ‡
		274 ‖ (children)	3-5 ‡
Fraction I	2,000	43 **	10 ‡
Gamma globulin	10,000	1,977 ††	0.05 ‡‡
Serum albumin, no heating	2,000	72 ††	1.5 ‡‡‡
Heating		103 **	0 ‡

* Vaughan, J.; Spurling, N., and Shone, J.: The Incidence, Incubation Period, and Symptomatology of Homologous Serum Jaundice, Brit. M. J. **1**: 409, 1946.

† Lewis, E. G.: Personal communication to the author: Results Obtained in a Survey Conducted by the Massachusetts Department of Public Health, with the Cooperation and Support of the American Red Cross.

‡ Preliminary results.

§ A few due to whole blood have been observed.

‖ Flynn, F.: Personal communication to the author.

¶ Loutit, B. M., and Maunsell, K.: Prevention of Homologous Serum Jaundice, Brit. M. J. **2**: 759, 1945.

Brightman, I. J., and Korns, R. F.: Homologous Serum Jaundice in Recipients of Pooled Plasma, J. A. M. A. **135**: 268 (Oct. 4) 1947.

** Hervey, G., and Diamond, L. K.: Personal communication to the author: Preliminary Data from American Red Cross Study.

†† Janeway, C. A., and Poole, V. S.: Unpublished data.

‡‡ One case each, probably not due to blood derivative.

many investigators who have cooperated in recent studies, for which blood derivatives have been provided by the National Blood Program of the American Red Cross.

17. Cohn, E. J.; Strong, L. E.; Hughes, W. L., Jr.; Mulford, D. L.; Ashworth, J. N.; Melin, M., and Taylor, H. L.: Preparation and Properties of Serum and Plasma Proteins: IV. A System for the Separation into Fractions of the Protein and Lipoprotein Components of Biological Tissues and Fluids, J. Am. Chem. Soc. **68**: 459-475, 1946. Mulford, D. J.: Derivatives of Blood Plasma, Ann. Rev. Physiol. **9**: 327-356, 1947.

1. *Products of Proteins Involved in Coagulation.*—The value of fibrin foam with thrombin as a hemostatic in many types of surgical procedure is well documented.[18] Whether the foam can be completely supplanted by "gelfoam" (absorbable gelatin sponge)[19] prepared from gelatin or by oxidized cellulose[20] is a problem which only time can solve. Whether potentially antigenic thrombin from animal sources should be used instead of human thrombin, which can be obtained in large amounts in any fractionation program, is a different problem. In any case fibrin foam with thrombin is one of a group of three types of absorbable hemostatic sponges, all of them effective, now available to surgeons in this country. Fibrin film, which has proved so valuable as a dural substitute in neurosurgery,[21] is being compared with film prepared from the plastic polyethylene.[22] Fibrinogen, which forms the matrix of the clot and constitutes 65 per cent of the protein of fraction I, has been used both topically and parenterally. Besides its use with thrombin as a means of attaching skin grafts,[23] it has been employed for the removal of renal stones in an ingenious procedure, whereby a solution of fibrinogen injected into the renal pelvis is coagulated with thrombin and the resulting clot drawn out with all its entrapped calculi.[24] Fraction I has been given in large amounts to several patients, whose blood totally lacked fibrinogen and who were suffering serious bleeding in consequence.[25] Here are instances in which, because of its low concentration in the plasma, it is impossible to give enough fibrinogen by whole blood or plasma transfusion, whereas with fraction I it has been possible to administer a dose equivalent to the total normal circulating fibrinogen.

Fraction I, although mainly composed of fibrinogen, also contains other proteins, including the substance which will rectify the coagulation defect in hemophilia; hence the term "antihemophilic globulin." Two hundred to six hundred milligrams of fraction I, reconstituted in 5 to 30 cc. of sterile water and given intravenously, will temporarily shorten the coagulation time in hemophilia in the same way as fresh blood or plasma.[26] Although this product has been proved effective for the temporary control of bleeding episodes and for preparation of patients for dental and surgical procedures, material of high potency can be prepared only from fresh plasma, because of the lability of this protein. Dosage figures will mean little until fresh plasma can be used as starting material and methods of assay can be better standardized.

2. *Blood Grouping Globulins.*—The anti-A and anti-B agglutinins as well as the anti-Rh agglutinins are globulins and can be concentrated as part of the fractionation procedure to yield blood grouping reagents of high potency; provided that the plasma pool from which they are prepared consists of plasma of a single type.[27] The need for readily available accurately standardized potent reagents for the vital blood grouping tests is fundamental to any blood program.

3. *Antibodies.*—The value of the gamma globulin fraction (fraction II) in the prevention and modification of measles was demonstrated in 1943 and 1944.[28] Since that time the use of gamma globulin for this purpose has become standard public health practice in this country. The extent to which a blood program will be called on to meet the need for this product can be inferred from the following figures. More than one million doses of gamma globulin surplus to the needs of the armed forces have been distributed by the Red Cross since 1944 and approximately 600,000 doses in the first six months of 1948 alone. Gamma globulin has been particularly useful in the control of measles in children's hospitals, because of its potency and safety.

Subsequently, the value of this fraction in the prevention and modification of epidemic hepatitis was likewise demonstrated in three outbreaks.[29] Table 3

TABLE 3.—*Summary of Results with Normal Serum Gamma Globulin in Common Diseases* *

Disease	Immunity in Infancy Early	Value of Globulin Prevention	Value of Globulin Treatment
Measles	+	+	±
Infectious hepatitis	—	+	0
Mumps	+	0	0
Scarlet fever	+	S	S
Poliomyelitis	+	—	0
German measles	+	S	—
Chickenpox	0	0	—
Infantile diarrhea	0	0	0
Homologous serum jaundice	—	S	—

Key: + Effective; ± questionable; 0 ineffective; — not known, and S under study.

* Reprinted from Cohn, E. J.: History of Plasma Fractionation, in Andrus, E. C.: Advances in Military Medicine, Vol. 1, Boston, Little, Brown & Co., 1948.

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summarizes present knowledge on the usefulness of gamma globulin in various infections.

Just as the potency of fraction I in hemophilia depends on the freshness of the plasma from which it comes, the antibody titer of a gamma globulin preparation will depend on the titer of the plasma from which it is derived. In certain instances—notably mumps and scarlet fever—antibodies are present in the blood of normal adults in relatively low titer. However, they are present in much higher concentration in the blood of patients convalescent from these infections, and gamma globulins from convalescent plasma will have a correspondingly higher titer (fig. 2). Such convalescent mumps gamma globulin has been shown to reduce the incidence of orchitis in adult male patients with mumps, although ordinary gamma globulin is ineffective.[30] In the case of pertussis, hyperimmunization of adults with Hemophilus pertussis vaccine has been used to obtain hyperimmune human serum for prevention and treatment of the disease. A gamma globulin concentrated from such plasma is being used instead of the bulkier serum, thus giving a much smaller dose for injection.[31]

4. *Serum Albumin.*—Serum albumin was originally developed as a blood substitute for the emergency treatment of shock in the wounded.[32] In this form it was dissolved in a twice-isotonic sodium chloride solution containing a mercurial bacteriostatic preservative. Subsequently its use in hypoproteinemic edema and nephrosis led to the preparation of a salt-poor albumin solution, in which the sodium content is one-seventh that of an osmotically equivalent volume of plasma and in which stabilization has made possible heating at 60 C. of ten hours.[33] This procedure, which has been shown to inactivate the virus of serum hepatitis,[34] and is adequate to destroy vegetative forms of many bacteria, permits the omission of the preservative. All albumin being produced now conforms to the specifications for low salt, mercurial-free serum albumin.

The value of serum albumin in the treatment of shock due to loss of blood depends on its effectiveness, convenience and safety. It suffers from the same defect as plasma, a lack of oxygen-carrying power, but does not transmit jaundice and is easier to transport and administer. Studies have indicated that in most cases of shock, unless additional sodium chloride solution is given (400 cc. to 25 Gm. of albumin) the full plasma volume increase of 18 cc. per gram of injected albumin will not be achieved, although on the average an increase of 10 to 12 cc. per gram will be observed.[35] However, the low viscosity of albumin makes it harmless even in concentrated solution.

During the past year and a half, distribution of serum albumin, prepared from surplus plasma which was pyrogenic or otherwise unsatisfactory, by the American Red Cross, has enabled investigators in teaching hospitals all over the country to study its physiologic and therapeutic value in a wide variety of conditions. The results of these studies will be summarized in a subsequent report, but some of the individual investigations are already in press or published.

Metabolic studies of the fate of albumin are laborious, but extremely important in understanding the relation between circulating albumin and the body protein stores. In rats, human serum albumin is an incomplete protein which must be supplemented with isoleucine and tryptophane if it is to promote growth and build new tissue protein.[36] Comparable studies in human beings have not been made. When fed to human subjects, serum albumin leads to an increase in nitrogen excretion such as would occur with any addition to dietary protein. When the albumin is injected, no such rise in nitrogen excretion occurs, and there is almost quantitative retention of the injected nitrogen. There

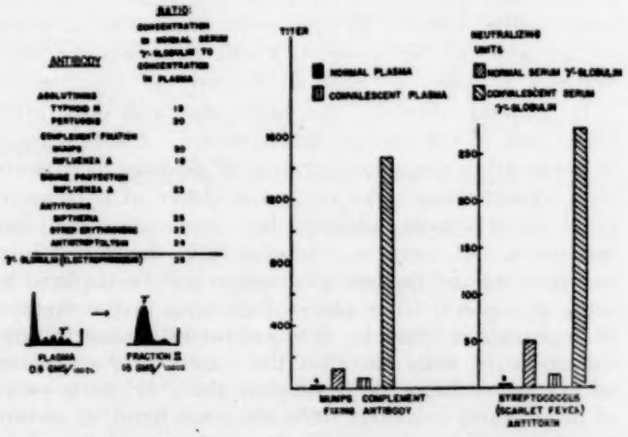

Fig. 2.—Concentration of antibody in normal serum gamma globulin and comparison between antibody titer of gamma globulin derived from normal plasma and that from mumps and scarlet fever convalescent plasmas.

is a rise in total circulating albumin and plasma volume which will account for only a portion of the injected protein.[37] Exactly where the remainder goes is an unsolved problem. The extent to which it is stored as albumin or smaller fragments in interstitial fluid or tissues, burned to yield energy or converted to tissue protein is under active investigation by several groups.[38] One interesting observation which has been made is that profuse albuminuria may develop when the concentration of albumin is pushed to abnormally high levels in patients with apparently normal kidneys.[39] Further studies will be needed to clarify the metabolic role of serum albumin.

The therapeutic indication for albumin is to sustain or restore the level of circulating albumin, if physiologic

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disturbances result from hypoalbuminemia. When the latter develops acutely, as in severe infections, burns, peritonitis or abdominal or thoracic operations, therapy is apt to be most effective. Large doses, 50 to 100 Gm. in twenty-four hours, and a high caloric intake, are needed to obtain maximum benefit. Albumin, which comes in 5 Gm. as well as 25 Gm. vials, is useful in pediatric patients because of its ease of administration, freedom from reactions and ready miscibility with other parenteral solutions. In some instances it has been used to mobilize fluid and relieve oliguria or to reduce local edema at such sites as the stoma of an intestinal anastomosis in patients with acute hypoproteinemia.[40] For its osmotic properties to be effective in getting rid of edema, the heart and kidneys must be capable of responding to an increase in plasma volume.

In chronic forms of hypoalbuminemia, the situation is more complex. In nephrosis, for example, the injected protein appears almost quantitatively in the urine and little elevation of the serum protein level follows daily injections.[41] Nevertheless, in my experience, many patients receiving an adequate dose of albumin, which is large and approaches the level of tolerance (15 Gm. a day under 4 years, 25 Gm. a day from 4 to 12 years of age and 50 Gm. over 12) will experience a slow diuresis as long as albumin therapy is continued.[42]

In general, diuresis has been observed only after about half of the courses administered. Caution must be observed in the administration of albumin to patients with hypertension. As yet, no evidence of permanent renal injury from albumin has been observed, but hematuria and nitrogen retention have developed in a few patients and further observation will be required to settle this point. The place of albumin in the therapy of nephrosis is limited. It is enormously wasteful and expensive; it does not alter the course of the disease, so far as we know, and subjects the child to a series of intravenous infusions. On the other hand, in certain cases in which other methods of therapy fail and in which edema is really incapacitating, my colleagues and I have found it useful. Rigid restriction of the sodium intake and the prevention and prompt treatment of intercurrent infections are essential in treating children with nephrosis.

The other major cause of chronic hypoalbuminemia is cirrhosis of the liver. Albumin therapy will elevate the serum albumin level to normal if daily doses of 50 Gm. are given for a period of one to two weeks.[43] This is followed by diuresis and disappearance of ascites in some patients, but not in others.[44] Two factors which seem to affect the results are the intake of sodium and the extent to which albumin accumulates in the ascitic fluid, thus raising its oncotic pressure. The most serious reaction observed has been hematemesis in a few patients with large esophageal varices.[32]

The value of concentrated albumin to relieve local or general edema of the brain in patients who have had cerebral trauma or operations is under study. Most neurosurgeons who have used it are convinced that it produces improvement more sustained than that following treatment with hypertonic dextrose, but more concrete evidence is needed before its general use is recommended.[45]

In this paper I have considered albumin as an inert colloid, given to restore osmotic relationships to normal. Presumably other colloids, such as globin, gelatin or gum acacia, might have the same effect. However, one must not lose sight of the fact that serum albumin is a physiologic substance, normally present in blood at a concentration of 4 to 5 per cent. Its osmotic function is best known, but serum albumin has been shown to have an important capacity, frequently rather specific, to bind, and thus presumably to transport in a physiologic manner, many substances of low molecular weight.[46] Thus, fatty acids,[47] naphthoquinones, such as the antimalarial drugs,[48] sulfonamide drugs,[49] mercury[50] and penicillin K[51] are substances for which these binding reactions have been studied. Moreover interactions of one plasma protein with another are just beginning to be investigated. Little clinical research has been devoted to this aspect of the function of albumin. It should not be forgotten, when the use of other substances having grossly similar osmotic properties is enthusiastically endorsed, that the fine structure of human serum albumin was developed by a long process of evolution to meet certain physiologic needs.

COMMENT

Two years ago this subject was presented before this assembly at the San Francisco meeting. At that time, it was pointed out that a large scale program of blood collection and processing would be necessary if physicians caring for our civilian population were to have the same opportunity for therapy and research with blood and its derivatives which was open to those connected with the armed forces during the war. During the past few years the American Red Cross has returned approximately four million packages of dried plasma and over one million doses of gamma globulin to the physicians of this country for the treatment of their patients. It has stimulated research on important practical problems, such as homologous serum jaundice, and has provided fraction I, gamma globulin, normal serum albumin and other blood derivatives to investigators all over the country for studies

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which have steadily expanded and defined the physiologic function and therapeutic value of many of the blood proteins. As the value of blood derivatives, prepared from a large backlog of surplus blood collected during the war, has been established and as that surplus has dwindled, the question of what would be done to provide these derivatives in the future has demanded an answer. A year ago, after prior consultation with and approval from the American Medical Association and other interested organizations, a National Blood Program was adopted by the American Red Cross. This program, not to be confused with the so-called permissive program, in which a local Red Cross chapter merely contracts to obtain donors for a community blood bank, is slowly getting under way. It is a broad program in which the collection of blood from voluntary donors in regional centers is used to meet the needs of local hospitals and physicians for whole blood and to supply material for processing to blood derivatives on the large scale required for economy. Research on methods of processing, on red cell preservation and on the development of new derivatives and the provision of material to qualified investigators are integral parts of this plan. Locally the medical supervision of the regional center is in the hands of a committee of the county medical society, as it should be, although obviously certain technical practices will have to conform to national standards. No regional center can be started without the approval of the local medical society, hospital association and health department. Such a program does not contemplate the destruction of existing local blood banks which are meeting the needs of the community, but is working toward supplementing them so as to provide not only a national network of blood banks in case of disaster but also the possibility of blood collection on the scale requisite to procure the amounts of blood and its derivatives needed to keep pace with advances in medical and surgical practice.

No better statement of the basis for the development and use of blood derivatives has been made than by Prof. Edwin J. Cohn,[46] whose researches have been responsible for the development of human plasma fractionation:

> Starting with the assumption, which must for the present remain an assumption, that every part of the human blood performs an important natural function—that the amount of any plasma component that may wisely be used in replacement therapy is the amount that will tend to reestablish rather than to derange the normal concentrations of the various physiologically significant plasma components—we have attempted to make available as many as possible of its diverse protein components, separated and concentrated as specific therapeutic agents, of value in different conditions, in the interest of the most effective and economical use by a society of the blood which it contributes.

SUMMARY

An attempt has been made to survey the field of blood derivatives. Like all active areas of investigation, it is in a state of flux. However, enough has been accomplished in a decade to establish certain derivatives, such as red cell suspensions, plasma, fraction I, fibrin foam with thrombin, fibrin film, gamma globulin, isohemagglutinins and serum albumin, as valuable therapeutic agents. The use of blood derivatives depends on an appreciation of the fact that deficiencies of one or another of the physiologic functions of the blood occur because of a lack of the specific components, usually proteins, which mediate them.

CLINICAL MANIFESTATIONS OF INFECTION WITH POLIOMYELITIS VIRUS

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Most of the clinical observations on poliomyelitis have been limited to that relatively rare form of the disease which results in residual paralysis. Even here no controlled observations have been published which enable one to say whether a great variety of symptoms are really typical of this disease. For instance, current articles in the foreign and American literature list diarrhea, sore throat, running nose and cough as symptoms of poliomyelitis, but offer no proof. It may be said with safety that outside of paralysis or paresis in a child with an acute febrile illness resulting in head drop, stiff neck and stiff back, and usually accompanied with moderate increase in the spinal fluid protein or cells, no symptoms have been firmly established. Children without these signs from whom the virus has been recovered have often been erroneously called "healthy carriers."

In the special survey of poliomyelitis which has been conducted in Chicago during the past three years, controlled field experiments were planned to elucidate the symptoms of all forms, but especially of the subclinical variety.[1] Subclinical poliomyelitis may be defined as poliomyelitis without stiff neck, stiff back, paralysis or obvious paresis. It is the common or usual manifestation in persons infected with this virus, and a comparison of the symptoms in the subclinical and clinical forms is herein presented.

MATERIAL AND METHODS

The material consists of 64 cases of subclinical and 33 of clinical poliomyelitis from twenty-one Chicago neighborhoods during 1945 and 1946. It was controlled by parallel observations on 157 noncontact or control children from the same

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Six tables giving clinical, epidemiologic and virologic data on the 254 children are included in the reprints, which are obtainable from the authors.

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neighborhoods, making a total of 254 children in the study. The neighborhood was that area within one block's radius of the residence of a reported paralytic case of poliomyelitis. The field [2] and laboratory [3] technics have been described.

Daily clinical observations, including axillary temperatures, were made on a number of children from the fifth to the twenty-first day after known intimate exposure to another child in the infectious stage (i. e., five days before to five days after the onset) [4] of poliomyelitis. Similar studies were made on noncontact subjects in the same and on controls in neighborhoods ten or fifty blocks distant. Noncontact subjects and control subjects were children of similar age and sex as the contact subjects but differing in that no intimate association could be established with another child in the infectious stage of either clinical or subclinical poliomyelitis.

Infection with poliomyelitis virus was said to have occurred if the virus could be recovered from the stool or throat (50 children), or if an elevation of the spinal fluid protein above 35 mg. occurred within twenty-one to forty-five days after exposure to the person with infectious disease. Two "noncontact" children from whom the virus was recovered (7 per cent) and their intimate contact sources were eliminated from this report as were a group of contacts from whom the virus could not be recovered or elevated spinal fluid protein demonstrated. Omitted are 30 contact children believed to have contracted subclinical poliomyelitis and from whom nose, throat and stool specimens were collected, which, at the time of reporting, had not yet been inoculated into monkeys. Several hundred other contact children from the same neighborhoods, but without the benefit of temperature, spinal fluid or virus data, likewise are omitted.

The stools to be tested were received by the virologists (F. B. G. and F. M. S.) in 50 per cent glycerin in isotonic sodium chloride solution and were emulsified in water and centrifuged at about 3,000 revolutions per minute for thirty minutes. The supernatant was dialyzed against distilled water at 4 to 8 C. for eighteen to twenty-four hours, removed and separated into two portions. One portion was designated "raw" and stored. The other portion was mixed with approximately equal volumes of absolute diethyl ether and shaken mechanically for twenty to thirty minutes. The ether was allowed to layer out, and the aqueous phase was cultured in a fluid thioglycollate medium. Specimens showing no bacterial growth in this medium after eighteen to twenty-four hours' incubation were considered to contain bacteria in numbers small enough to allow inoculation of monkeys. Specimens were shaken daily with ether until the point of concentration of viable bacteria described previously was attained. The aqueous phase was drawn off and residual ether removed under decreased atmospheric pressure. All specimens were stored in a frozen state of approximately —20 C. until inoculated into monkeys.

Three species of monkeys were used in the study: (1) Macaca mulatta (Rhesus), (2) Macaca cynomolgus and (3) Cercocebus fuliginosus (sooty mangabey). Each specimen was tested for virus by inoculation of 2 monkeys by the following routes: intracerebral and intraperitoneal inoculation with the ether-treated material and intranasal inoculation with the "raw" material. Daily temperature records and observations were made on each animal for a period of twenty-one days (or until clinical signs of poliomyelitis were obvious), at which time the animals were killed and representative samples of the neuraxis were taken for histologic examination.[5]

Throat specimens were treated exactly as the stool specimens except that the preliminary emulsification and centrifugation were omitted.

2. Casey, Fishbein and Bundesen.[2a] Andelman, Fishbein, Casey and Bundesen.[2b] Casey, Fishbein, Abrams and Bundesen.[2c] Casey.[2d] Casey, Fishbein, Abrams, Drucker, Rubinfine, Lava and Bundesen.[2e]

3. Schabel and Gordon.[3c] Gordon, Schabel, Casey and Fishbein.[3f] Gordon, Schabel, Casey, Fishbein and Abendroth.[3g]

4. (*a*) Casey.[4d] (*b*) Gordon, Schabel, Casey and Fishbein.[3f] (*c*) Casey, A. E.: Observations on an Epidemic of Poliomyelitis, Science **95**: 359-360 (April 3) 1942. (*d*) Aycock, W. L., and Kessel, J. F.: Infectious Period of Poliomyelitis and Virus Detection, Am. J. M. Sc. **205**: 454-465 (March) 1943.

5. Schabel and Gordon.[3c] Gordon, Schabel, Casey and Fishbein.[3f] Gordon, Schabel, Casey, Fishbein and Abendroth.[3g] Casey, Fishbein, Abrams, Drucker, Rubinfine, Lava and Bundesen.[2e]

The virus of poliomyelitis was recovered from stools collected during the observation period on 50 of the contact children; 10 other contact children in the field study (4 of whom had not yet been tested for virus) had delayed spinal fluid protein values elevated above 35 mg. Eight additional children who had had intimate contact with infectious patients in the same neighborhoods were recovering or had recovered from minor illnesses without paralysis or stiff neck when the study began. The spinal fluid protein values were elevated above 35 mg. in each. The illness in 4 of the 60 contact subjects in the field study was associated with stiff neck, in 1 with paralysis. Sixty-four children, none of whom had stiff neck, stiff back or paralysis, are considered to have had subclinical poliomyelitis.

There were 33 children from the twenty-one neighborhoods (the 24 original subjects with paralytic disease which attracted us to the particular neighborhoods for a field study and 9 with clinical conditions discovered in the neighborhoods by the field study including the 4 previously mentioned). Each patient with clinical poliomyelitis was admitted to a hospital where thorough clinical and laboratory studies were made (29 were admitted to the Municipal Contagious Disease Hospital, under the direct supervision of Drs. Archibald Hoyne and R. Brown and their staff, and 1 each to Cook County, Children's Memorial and Evanston hospitals).

As already mentioned there were 157 noncontact and control children in the study. Virus was not recovered from the stools, and the spinal fluid protein was not found elevated in 33 noncontact and control children from the same neighborhoods about whom careful field studies failed to establish association with a clinical or subclinical case of poliomyelitis in the infectious period.

Since virus was found in only 7 per cent of the noncontact children examined we added as controls 124 additional children from the same neighborhood studies. Thirty-three were noncontact children of whom temperature and field studies were carried out and from whom nose, throat and stool specimens were collected, but not yet used for inoculation in monkeys; 43 were control children from the 1945 studies and 48 control children from the 1946 studies. These children resided ten or fifty blocks distant from the thirteen poliomyelitis neighborhoods and were chosen for the purpose of sampling virus distribution in the city and for comparing illnesses in such children with those occurring among the noncontact children in the same block as the poliomyelitis patient. The inclusion of these 124 children possibly adds 5 to 8 children from whom poliomyelitis virus may be obtained when our animal inoculations are completed. However, such a small group should not significantly affect our comparative results except to diminish rather than to add to the significance of the symptoms.

Because we wanted to avoid biased clinical observations in our field studies we enlisted the aid of four pediatricians with special training in poliomyelitis (Martin B. Andelman, Irving Abrams, Herman Lander and Arnold P. Drucker), who checked in the neighborhood or in the hospital every illness and suspected illness among the 254 contact, noncontact and control children whose case histories are herein reported. They examined carefully for paresis, paralysis, reflex changes, head drop, stiff neck, stiff back and other clinical features. In addition, each contact, noncontact and control child had, during the period of five to twenty-one days after known exposure to an infectious patient, daily axillary temperature taken and nose, throat and stool specimens collected, and clinical observations were recorded by the field nurses and the field investigators. (The nurses chiefly responsible were Minnie Altiere, Arlene Ross, Audrey Korwin, Lydia Goltz, Florence Brock and Amy Quinlan.) All the children in each of the contact and control neighborhoods herein reported were personally investigated by the senior author, usually by many repeated visits to friends, neighbors and families.

RESULTS

There was no significant difference in the incidence of fever, leg ache, headache, sore throat, vomiting, constipation, diarrhea, running nose, cough or drowsiness

between the noncontact patients in 1945-1946 the results for whom were negative for virus and elevated spinal fluid protein and the 43 control subjects for 1945, the 33 noncontact patients for 1946 and the 48 control subjects for 1946, none of whose stools had been injected into monkeys. Three children in the 1946 control group said to have been listless in the field protocols were classified as drowsy, and this error was shown in the calculations. Also, in 4 of the 1945 subjects pertussis developed during the study, and vomiting was therefore prominent. Since the symptoms in the various control and noncontact groups were essentially homogeneous, these were combined in order to swell the controls for the comparisons with the symptoms in children from whom virus was recovered.

The incidence of the various symptoms and signs in the 157 control and noncontact children was compared with the incidence of various symptoms and signs in the 64 contact children with subclinical poliomyelitis. Fever (almost invariably mild), headache, constipation and drowsiness occurred significantly more often among the children with subclinical poliomyelitis than among the control group. Vomiting, though only probably significant in the entire group, was statistically significant when the 4 pertussis cases were eliminated, or when the incidence was compared directly with that in the 33 noncontact and control children already tested for virus.

Noteworthy was the fact that sore throat, diarrhea, running nose and cough were not significantly related to the symptoms of subclinical poliomyelitis. There was evidence that diarrhea, running nose and cough were significantly not related to this disease. Leg ache was observed too infrequently to be of significance.

The symptoms in the patients with clinical poliomyelitis were then compared with those in the control group. Again running nose, diarrhea and cough were not symptoms of clinical poliomyelitis, but sore throat and leg ache were. The symptoms of headache, vomiting, constipation, drowsiness and mild fever were of statistical significance as in the subclinical form. The difference was that headache, vomiting, constipation, drowsiness, fever and leg ache were more often encountered in the clinical than in the subclinical form. It is interesting that sore throat had no relation to the symptoms of the patients with the subclinical form of poliomyelitis but was often present in children who had stiff neck, stiff back, head drop and paralysis. Furthermore, careful notations at the Municipal Contagious Disease Hospital illustrate the frequency of a visibly red throat in the clinical form. If aches in the muscles of the abdomen and upper extremities were added to those of the lower extremities, myalgia would be a significant symptom in the subclinical as well as the clinical form. Pain along the cervical part of the spine was not infrequent.

COMMENT

Of the 64 children with subclinical poliomyelitis, 16 (25 per cent) presented no symptoms or signs of fever, headache, vomiting, constipation or drowsiness; 8 additional children had fever detected only by the nurses' taking the daily axillary temperatures and not recognized by the patient or by the mother. This made a total of 24 children (38 per cent) who had no reported subjective symptoms whatever. Twenty-two of the 24 children without professed symptoms were 6 years of age, or under (92 per cent), whereas only 24 of 40 children with symptoms were 6 years of age or under. This difference is statistically significant ($X^2 = 7.4$; $n = 1$; $P = 0.01-$).

To determine whether the subclinical illness was less severe among the preschool children than among those over 6 years of age, the 39 children without history of prior illness or fever were analyzed. Fever was observed by axillary temperature determinations in 5 of 9 children over 6 years of age and in 16 of 30 children 6 years of age and under. Fever was of almost identical incidence in the two groups ($X^2 = 0.013$; $n = 1$). It would seem, therefore, as one might expect, that the preschool children were not as accurate in reporting their symptoms as the older children. An error in our field method was detected in that mothers sometimes noted, with their own thermometers, fevers in the evenings in children when normal readings were made in the nurses' daily visits. These evening fevers were more frequent among the contact than among the control children, and we would recommend afternoon and evening temperature readings for three weeks after exposure to an infectious patient.

The incidence of 1 case of paralytic disease (2 per cent) and 3 of meningitic disease (5 per cent) to 56 cases of subclinical disease (93 per cent), as determined by the virus study, is in close accord with the estimates derived from the field histories and temperature studies already published.[6]

Current studies by our group (unpublished material) on the incidence of stool versus mouth and throat virus in children with the clinical and subclinical disease indicate that the stool virus is present in both groups in apparently the same frequency. However, the virus was recovered from the throat in each of the aforementioned 4 paralytic and meningitic patients (100 per cent) with the clinical disease tested in the last five days of the incubation period and in only about 33 per cent of children with the subclinical form of poliomyelitis.[7] This may explain why sore throat is a symptom of the clinical but not of the subclinical variety. It may also explain why it was possible in earlier studies in Walker County, Ala., to trace a paralytic or meningitic case to contact with a prior paralytic or meningitic case with more ease than to a prior subclinical case.[8] It might also explain why poliomyelitis seems to burn out in a given neighborhood or area if transmission is largely through clinical cases. This would seem to substantiate the importance of the throat and mouth in the contact transmission and minimize the importance of the stool virus in modern communities. This need not predicate that the virus is not present in the throat in the usual subclinical case, but only that it is not easily recovered by swabs or transmitted to another child. Perhaps the severity of throat symptoms is usually directly proportioned to the amount of virus present in the throat and underlying nervous system.

Acute febrile illnesses, without paralysis, of sudden onset and of eighteen to seventy-two hours' duration, among the contacts of poliomyelitis patients have long

6. Casey, Fishbein and Bundesen.[1a] Andelman, Fishbein, Casey and Bundesen.[1b] Casey, Fishbein, Abrams and Bundesen.[1c]

7. Schabel, F. M.; Casey, A. E.; Fishbein, W. I., and Gordon, F. B.: Unpublished data.

8. Casey.[4c] Schabel, Casey, Fishbein and Gordon.[7] Casey, A. E.: The Pathology of Poliomyelitis with Special Reference to Observations in Walker County, Alabama, J. M. A. Alabama **12**: 2-3 (July) 1942; The Incubation Period in Epidemic Poliomyelitis, J. A. M. A. **120**: 805-807 (Nov. 14) 1942; Place of Contact and Radial Spread of Epidemic Poliomyelitis, Am. J. Dis. Child. **69**: 152-156 (March) 1945. Wenner, H. A., and Casey, A. E.: A Community Study of Carriers in Epidemic Poliomyelitis, J. Clin. Investigation **22**: 117-125 (Jan.) 1943.

been recognized.[9] The symptoms of headache, vomiting, sore throat, malaise, drowsiness, reddened throat and enlarged lymph nodes have been described. Estimates of the frequency of such cases have gradually increased during the years: 1:1 or 2:1,[9a] 2:1 or 4:1,[9c,d] and 6:1 or 14:1.[9e] Because the head drop, stiff neck and stiff back were so characteristic, no clinical diagnoses of nonparalytic poliomyelitis were generally considered tenable without these observations. The other symptoms have been considered too speculative for clinical use.

The literature contains only isolated instances of minor illnesses among contact subjects without stiff back, stiff neck and without paralysis, which were proved by the recovery of the virus or by demonstration of a rise in spinal fluid protein. Taylor and Amoss[9g] in 1917 recovered the virus from the throat of a child contact (white boy, aged 10 years) several days before fever of short duration and diarrhea developed. There was no stiff back, stiff neck or paralysis and no other symptoms. Paul and Trask[9e] recovered virus from the throat of 2 contact subjects without paralysis or stiff neck. The first, a white male infant of 13 months, had fever and drowsiness and the reaction of the spinal fluid was negative immediately; the second, a white boy aged 5 years, had fever of eighteen hours' duration and vomiting. Paul, Trask and Webster[9h] obtained the virus from the throat of a contact subject in whom nausea, headache, fever, anorexia and pains in the legs and back developed, with the immediate reaction of the spinal fluid negative and no stiff neck, stiff back, paralysis or weakness. Langmuir[9i] recovered virus from the stool of 10 contact subjects without stiff neck, stiff back or paralysis. Four of the 10 experienced vomiting and abdominal pain, 1 fever and vomiting, 1 pain in the knees and backache and 1 headache, pain in the eyes, dizziness and soreness in the chest and abdomen; 2 had "mild upper respiratory symptoms" and were not confined to bed. Of the 14 children described, 5 had fever of short duration, 6 experienced vomiting, 2 headache, 4 abdominal pain, 2 pains in the legs and 2 pains in the back. The low incidence of fever may be due to the lack of systematic field study, and the high incidence of other symptoms to the failure to study the stools of many asymptomatic infants for virus. The symptoms detected are entirely compatible with our own observations.

Ours is, however, the first controlled series of children with subclinical poliomyelitis studied during the incubation and disease periods and proved by virus and spinal fluid studies.

SUMMARY AND CONCLUSIONS

The symptoms reported by 97 children with poliomyelitis are compared with those among 66 noncontact children living in the same block with the patients, and among 91 control children living in neighborhoods ten or fifty blocks distant. Poliomyelitis was proved in each child by the recovery of virus from the stool or throat and/or by the occurrence of elevated levels of spinal fluid protein twenty-one to forty-five days after intimate contact with an infectious patient.

Thirty-three of the 97 had clinical poliomyelitis characterized by paralysis, paresis, head drop, stiff neck or stiff back. The remaining 64 were intimate contacts of infectious patients in whom subclinical poliomyelitis characterized by an absence of the aforementioned signs developed within five to twenty-one days after exposure.

No differences in the symptoms between the noncontact children and the controls were detected. Mild fever of short duration, headache, vomiting, constipation, myalgia and drowsiness characterized both the clinical and the subclinical forms of poliomyelitis, the difference being one of degree and increased frequency among the former. Sore throat was definitely not a symptom of the subclinical variety, but was significantly related to stiff neck, stiff back and paralysis or paresis. The possibility is discussed that the presence of sore throat in clinical cases and its absence in subclinical cases might coincide with the quantity of virus present in the throat and in the nervous system, with the infectiousness and clinical severity and with certain epidemiologic features of the disease.

Running nose, diarrhea and cough were definitely not related to the symptoms of either clinical or subclinical poliomyelitis. Evidence of poliomyelitis among children 6 years of age and under is difficult to obtain without an adequate field study, even though 80 to 100 per cent of such children succumb on exposure. The younger patients are less likely to report minor symptoms described in almost every instance by older children.

Virus was recovered from the stool (50 children) and/or the spinal fluid protein was elevated above 35 mg. in 60 intimate contact sources of infectious patients in whom poliomyelitis developed within five to twenty-three days after known exposure. Four of the 60 children had the clinical disease (1 was paralytic [2 per cent] and the other 3 nonparalytic [5 per cent], with stiff neck, stiff back and head drop) and the remaining 56 had the usual or subclinical form of the disease (93 per cent).

ABSTRACT OF DISCUSSION

DR. HULDA E. THELANDER, San Francisco: Subclinical poliomyelitis in the environment of the paralytic patient is the logical clinical concept. The infectious agent is widely dispersed, but only a relatively small number of persons harboring the virus succumb to recognizable disease. This knowledge should alert one to considering more carefully the host and factors influencing susceptibility on the one hand and the possible variability of the infectious agent on the other. The literature makes frequent references to fatigue and trauma as factors predisposing the host to paralytic disease. Dr. Shaw and I have long maintained that bacterial infections at times may also be predisposing factors. Most of the cases in any epidemic season are almost completely devoid of any apparent infections of the respiratory or the intestinal tracts. There are, however, some patients with exudative sore throat or with diarrhea, and even pneumonia, preceding paralytic symptoms. It is likely that these symptoms represent concomitant infections which may actually alter the host's resistance to the virus of poliomyelitis. Such infections may even be the explanation of the so-called dromedary type of the disease. From experi-

9. (*a*) Wickman, I.: Beiträge zur Kenntnis der Heine-Medinschen Krankheit (Poliomyelitis acuta und verwandter Erkrankungen), Berlin, S. Karger, 1907. (*b*) Peabody, F. W.; Draper, G., and Dochez, A. R.: A Clinical Study of Acute Poliomyelitis, Monograph 4, Rockefeller Institute for Medical Research, June 24, 1912. (*c*) Frost, W. H.: Epidemiologic Studies of Acute Anterior Poliomyelitis, Hygienic Laboratory Bulletin 90, United States Treasury Department, Public Health Service, 1913. (*d*) Leake, J. P.; Bolton, J., and Smith, H. F.: Winter Outbreak of Poliomyelitis, Pub. Health Rep. **32**: 1995-2015 (Nov. 30) 1917. (*e*) Paul, J. R., and Trask, J. D.: Observations on Epidemiology of Poliomyelitis with Particular Reference to So-Called "Abortive" Poliomyelitis, Tr. A. Am. Physicians **47**: 116-128, 1932; Detection of Poliomyelitis Virus in So-Called Abortive Types of the Disease, J. Exper. Med. **56**: 319-343 (Sept.) 1932. (*f*) Aycock, W. L.: Acute Anterior Poliomyelitis, in Nelson's Loose Leaf Medicine, New York, Thos. Nelson & Sons, 1943, vol. 2, pp. 67-84. (*g*) Taylor, E., and Amoss, H. L.: Carrier of Virus of Poliomyelitis, J. Exper. Med. **26**: 745-754 (Nov.) 1917. (*h*) Paul, J. R.; Trask, J. D., and Webster, L. T.: Isolation of Poliomyelitis Virus from Nasopharynx, J. Exper. Med. **62**: 245-257 (Aug.) 1935. (*i*) Langmuir, A. D.: Carriers and Abortive Cases in a Rural Poliomyelitis Outbreak, Am. J. Pub. Health **32**: 275-281 (March) 1942.

ments in animal passage, it is evident that viruses may alter their characteristics. How much human passage may result in alterations of the virus has not been determined. Does the present concept of poliomyelitis represent more accurate observations of the disease, or has the disease altered some of its manifestations through the years? This possibility should be carefully evaluated in recording observations for comparison with future studies; accurate clinical observations may contribute as much to progress in our knowledge of the disease as laboratory studies.

DR. JAMES P. LEAKE, Washington, D. C.: Poliomyelitis occurs at all times and in all places, permitting comparison of one epidemic area with another, but for comparison of the incidence in various climates and places, I think that one can count only paralytic cases, that is, cases in which there is definite demonstrable muscular weakness. As far as I know, this is the first time the incidence of symptoms has been statistically worked out. We are indebted to Drs. Casey, Bundesen and McCoy and all others that have labored so thoroughly on this. Their results coincide with what we have felt before. Dr. Thelander's caution of considering at least the possibility that many things that are usually attributed to a disease may be a preceding infection is worth taking into consideration.

DR. C. H. WEBB, Shreveport, La.: While the varied manifestations of infection with poliomyelitis virus and the frequency of subclinical disease are generally recognized, the need of definitive studies is evidenced by vague statements in the literature; for example, that in every epidemic 10 to 1,000 cases of mild disease occur for every case with paralysis. The incidence of subclinical infections reported by the authors among the contacts as compared with noncontact children in the same neighborhood connotes important epidemiologic implications. The charts of 50 children whose disease was diagnosed as acute poliomyelitis by four pediatricians in the group observed by my co-workers and me were reviewed: 45 of these children have been seen since 1940; 33 were paralytic and 17 nonparalytic. Fever was listed in every instance, headache in 30 per cent, irritability in 32 per cent, sore throat or reddened pharynx in 28 per cent and drowsiness in 14 per cent. No significant variation was noted in these symptoms as between paralytic and nonparalytic children. Leg ache was complained of by 25 per cent of the paralytic patients, but by none of the nonparalytic. Vomiting occurred in 33 per cent of the paralytic patients and in only 12 per cent of the nonparalytic. Abdominal pain and constipation were noted in 15 and 9 per cent of the paralytic and rarely in the nonparalytic children. Diarrhea, coryza and cough were listed in less than 5 per cent of either group. It is worthy of note that convulsions occur rarely in poliomyelitis—only once in our 50 cases, in striking contrast to other acute infections of the central nervous system during childhood. During the summer of 1947, diagnostic difficulties were presented by the occurrence of a clinical syndrome of epidemic proportions, consisting of sudden high temperature, headache and occasional myalgia, lasting three to four days and clearing dramatically. Symptoms referable to the gastrointestinal or respiratory tract were rare. Successive sibling or contact cases suggested an incubation period of four to seven days. Adults were infrequently affected. Treatment with sulfonamide drugs or penicillin, when tried, was unavailing; laboratory observations were equivocal. In several instances, questionably stiff neck or back pains prompted spinal fluid examinations, results of which were normal. During the same period, in which we have records of 48 such cases and knew of over 100 more, poliomyelitis was at low ebb and no contact history could be established. We believe that this is a separate entity, probably of virus causation, and have recently described its clinical and epidemiologic features under the name "three day fever." It is intriguing to note its similarities to nonparalytic poliomyelitis and to herpetic pharyngitis, and yet distinctive features appear. It is hoped that virus studies can be made if a similar epidemic occurs. From the point of view of clinical research and experience, it would be important to evaluate all available methods by which viral infections may be differentiated from bacterial, in view of the general tendency to administer sulfonamide drugs and antibiotics to all acutely ill children. We are pursuing a study of atypical lymphocytes, heretofore described in infectious mononucleosis, measles, german measles and infectious hepatitis. To a varying degree we find that these cells occur in a number of infections in which the cause has been demonstrated or presumed to be viral, but rarely in bacterial infections.

DR. HADDOW M. KEITH, Rochester, Minn.: Subclinical poliomyelitis is recognized only by recovering the virus from stools or from the throat or when the level of spinal fluid protein is elevated, other causes for this, of course, being ruled out. The method of proving subclinical infections is available mainly to groups having facilities to recover the virus; in other words to specially organized, trained and endowed groups. Perhaps the majority of children, then, have a mild form of subclinical poliomyelitis and therefore have immunity for a good many years. It has also been suggested that in crowded and unsanitary areas in the East, such as Cairo and Bombay, poliomyelitis is not a major problem, but in our American cities it has tended to increase within the past fifty years. Also there tends to be more poliomyelitis and severer poliomylitis in adults than there used to be. Are we by our effective public health measures against other diseases making poliomyelitis more of a problem than it used to be? If so, this means that we must direct our efforts toward a program of prevention, such as we conduct against smallpox or diphtheria. I would like to point out that neutralizing antibody tests reveal different strains of poliomyelitis virus, which may make a preventive program a little more difficult. I think that it is also true that the correlation of neutralizing antibodies and clinical immunity is not absolute and further studies are necessary along these lines. There is no doubt that there are numerous problems to be solved before poliomyelitis can be controlled effectively. It seems imperative, however, that the main effort be directed toward developing preventive procedures applicable in infants and children, such as have been developed against the other great epidemic diseases.

DR. A. F. ABT, Chicago: The definitions submitted for subclinical and clinical poliomyelitis rather confused me. Of course, in pediatrics, there are continually changing definitions, with resultant confusion, but the long accepted definitions, as I knew them, consisted first of reported poliomyelitis, which is understood to be a systemic infection with no involvement of the central nervous system. Then comes a period of quiescence of symptoms, following which there is again fever, and then, as I take it, there are two types of infection—the nonparalytic and the paralytic. In the abortive type with systemic infection and no involvement of the central nervous system there is a clear normal spinal fluid, and we have no way of making a positive diagnosis of this type. What is needed is a quick and rapid method of isolating the virus, so that if one could distinguish this systemic involvement without involvement of the central nervous system, then one could probably evolve some form of treatment, but I do not feel that the treatment will ever be effective in the nonparalytic or paralytic stages.

DR. ALBERT E. CASEY: The point made by Dr. Thelander on the symptoms of concomitant infection and constitutional variation may explain some of the problems in this disease. The importance of differentiating between infection with stiff neck from infection without stiff neck is borne out by current studies in our group. This is unpublished material on the incidence of stool versus mouth and throat virus in children with the clinical and subclinical difficulties. These indicate that the stool virus is present in both groups. However, the virus was recovered in the throat in each of the aforementioned paralytic and meningitic patients but in only about 33 per cent of children with the subclinical form of poliomyelitis. This may explain why sore throat is a symptom of the clinical but not of the subclinical variety. It might also explain why poliomyelitis seems to burn out in a given neighborhood with transmissions largely from subjects with clinical infection. This would seem to substantiate the importance of throat and mouth and contact infection and minimize the importance of transmission in schools in the modern communities.

TREATMENT OF IDIOPATHIC PERNICIOUS ANEMIA

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Addisonian or idiopathic pernicious anemia is a complex disease resulting from a lack of specific factors necessary (1) for the normal growth and development of erythrocytes, (2) for the nutrition of nerves and spinal cord and (3) for the correct functioning of the gastrointestinal tract. With a deficiency of such factors (1) large uncompleted red cells stagnate in the marrow which becomes hyperplastic and red—such erythrocytes as are released into the circulation are macrocytic and so larger than normal, (2) the peripheral nerves and spinal cord degenerate from interference with nutrition and (3) the papillae of the tongue atrophy and the epithelial cells of the gastrointestinal tract become abnormal with impaired function. It is not known just how many factors are involved. There are certainly two and perhaps more. The disease was always fatal before the discovery of liver therapy. Over 10,000 persons died yearly in the United States alone before the epoch-making work of Whipple, Minot, and Murphy.

The clinical features of the disease are (1) macrocytic anemia, determined by count and measurement of the red cells, (2) subacute combined sclerosis of the spinal cord and peripheral neuritis, usually manifested first by a loss of vibratory sense, and (3) atrophy and soreness of the tongue, often diarrhea and digestive disturbances from impaired function of the stomach and intestinal tract, and a constant and absolute absence of free hydrochloric acid on gastric analysis. Not all patients show every manifestation. The combinations of symptoms and signs are varied; all, however, show the macrocytosis of red cells and achlorhydria. The patient is completely relieved of active disease by adequate liver therapy.

THE BONE MARROW LESION

In true idiopathic pernicious anemia there is a gradual lack of the specific factor needed for maturity of the red cells in the bone marrow. More young and incomplete erythrocytes which are larger than normal appear in the circulation. The number of circulating cells decreases also, so that there is macrocytic anemia. As the deficiency continues more and more immature large cells accumulate in the marrow, and the anemia of the peripheral blood becomes more pronounced. The examination of the bone marrow obtained by puncture shows many large megaloblasts and other macrocytes. The peripheral erythrocyte count becomes lower and lower. As the anemia progresses, the red cells continue large, and in time other abnormalities, such as poikilocytosis, anisocytosis, nucleated cells and basophilia, appear. These are late manifestations, however, and one should never wait for their appearance before making the diagnosis of pernicious anemia. The diagnosis should be made on the basis of manifestations of which the most important, so far as the blood is concerned, is the macrocytosis of red cells.

From the Cleveland Clinic and Frank E. Bunts Educational Institute.
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With macrocytic anemia there is usually leukopenia with increased maturity of the polymorphoneutrophilic cells. The leukocytes are retained in the hyperplastic red cell tissue longer than normal and thus become more mature, as shown by increased segmentation of the nucleus. Similarly, the development of megakaryocytes is interfered with and the number of platelets in the peripheral blood is reduced. The characteristic blood lesion then is macrocytic anemia with leukopenia and reduced platelet count.

THE NEUROLOGIC LESION

A high proportion of patients with well developed pernicious anemia complain of numbness and tingling of the hands and feet. Examination reveals that the vibratory sense in the lower legs is impaired. Later this becomes more widespread, the position sense of the feet is lost and still later there may be ataxia or spasticity with altered tendon reflexes due to impairment of the posterior and lateral columns of the spinal cord. Many patients with unrecognized or inadequately treated disease become unable to walk and are confined to bed.

THE GASTROINTESTINAL LESION

An almost constant observation in untreated or incompletely treated pernicious anemia is a clean smooth tongue, due to atrophy of the papillae. With this atrophy, real glossitis develops. This also is due to the lack of specific factors necessary for the normal nutrition of the tongue.

There is always achlorhydria. This seems a primary lesion with atrophy of the mucosa of the stomach and subsequent loss of gastric ferments. Many available data indicate that a patient with pernicious anemia has always lacked free hydrochloric acid. Every patient suspected of having pernicious anemia should have a test meal as well as careful study of blood and bone marrow. The mucosa of the small bowel also becomes atrophic and does not function normally. Absorption is faulty, leading to digestive disturbances and impaired nutrition. Diarrhea often develops.

The deficiency in pernicious anemia is quantitative. If untreated, it gradually becomes worse, with more serious symptoms. The blood lesion can be completely reversed with a return of the blood to normal. The anemia, leukopenia and thrombopenia all disappear, leaving no trace of the former deficiency. The bone marrow also becomes normal. The achlorhydria is permanent. Free hydrochloric acid never reappears in the stomach, regardless of intensive therapy.

COURSE OF EVENTS IN PERNICIOUS ANEMIA

The primary defect in pernicious anemia is a deficiency in a secretion of the stomach mucosa, the intrinsic factor of Castle, which acts on ingested food to form the substance or substances necessary for normal nutrition of bone marrow, nervous system, tongue and gastrointestinal tract. The intrinsic factor is probably a ferment.

Liver therapy completely relieves the deficiency in all three systems. This was at first thought due to a direct supply by the liver of a maturing factor or factors. It seems apparent that liver extract acts through some other mechanism and not by actually furnishing the missing factor or factors.

The discovery of folic acid throws further light on the problem. It has been observed that this may replace liver extract in relieving the anemia and thus may be the specific erythrocyte-maturing factor missing in the bone marrow. It may become a part of the erythrocyte

stroma. Potent liver extract contains only a minimum of folic acid and not enough for the action observed. Moreover, it does not protect against a neurologic lesion, so that it is evidently not the specific element needed for the nutrition of nerve tissue. It may cause the gastrointestinal tract to return to normal. It seems probable that liver extract acts through an enzyme system enabling the body to release the specific principles needed from stores of bound substances in the body. This explains its action in relieving all the deficiencies involving the blood, nervous system and gastrointestinal tract without actually supplying the needed substances.

The defect arising primarily in the stomach in true addisonian pernicious anemia may arise secondarily in other diseases, such as sprue, or after operation on the gastrointestinal tract. Here the defect is not due to lack of formation but to lack of absorption or utilization or to increased need, as in pregnancy.

How should this complex deficiency which is called pernicious anemia be treated? In idiopathic pernicious anemia the initial defect is permanent. There is no evidence that the missing factor in the stomach, which is primarily at fault, ever returns. Treatment must be adequate and permanent. The amount of deficiency is variable, so that it is difficult to gage the need. The important point in therapy is to treat fully and permanently. Since one cannot accurately gage the need for specific treatment, it is best to give enough treatment to cover all possible needs. Overtreatment does no harm, while undertreatment often leads to serious disability. Often less treatment is required to relieve the blood lesion than is needed to prevent or relieve the neurologic lesion. Every student of the disease is constantly confronted with patients who have had enough treatment to prevent significant anemia but present a disabling cord lesion while the insufficient treatment is being carried on. Since the cord lesion may be irreversible, often the patient remains a cripple regardless of the intensity of treatment.

The degree of involvement of the three systems is variable. There may be little anemia with much neurologic disturbance. The anemia may be extreme with no demonstrable neurologic disturbance; thus all combinations are possible.

Many methods of treatment are now available—whole liver, oral liver extracts, parenteral liver extracts, stomach extracts, folic acid and accessory substances, such as iron, hydrochloric acid and vitamin preparations, are offered for selection. The suggestions given are based on experience with more than 600 patients with true addisonian pernicious anemia by one of us (R. L. H.) and on recent discussions with numerous hematologists having a wide interest in this disease.

Whole liver is an excellent source of protein food besides having the specific action of liver. It is helpful for a person suffering from pernicious anemia to include liver in the diet, but it is not satisfactory for complete treatment. Stomach extracts can be given only orally, so that they are not desirable for the treatment of pernicious anemia. Oral liver extracts are often disagreeable to take, are much less potent than parenteral liver extracts and depend on absorption from the gastrointestinal tract. Treatment with oral liver extract is also more expensive than parenteral therapy.

Parenteral administration of liver extract is the treatment of choice for pernicious anemia. Unfortunately, extracts of many different unitages are offered the physician. The most desirable extract contains 15 antianemic units per cubic centimeter. It has been found difficult to make preparations of more potency. There is no reason to use a weaker extract, such as 1, 2, 5 or 10 units, or stronger extracts, containing more than 15 units per cubic centimeter. The problem is complicated only by using extracts of low and varying potency. These are provided entirely to meet competition among drug houses and not to supply real needs of the patient. Unfortunately, all liver extracts have to be standardized on patients. It seems evident that a unit is not always the same, although theoretically it represents the daily need. It is important to select a potent extract containing 15 units per cubic centimeter and to continue the use of this preparation, since one soon learns what to expect from a preparation of dependable constancy.

How should this liver extract be prescribed? There is no way to determine exactly the amount of specific principle needed to supply the deficiency. Any excess given is not excreted, and when treatment is begun the body is usually completely void of the needed factor. It is doubtful whether symptoms develop until the deficiency is absolute. The results of incomplete therapy are serious, often leading to permanent disability from a cord lesion, and overtreatment is always indicated. There is no harm in overtreating, and additional liver extract is inexpensive. The first principle in treatment is to prescribe large amounts for a sufficiently long time. There is no way to be exact in dosage. We insist, if possible, in hospitalizing the patient for the first two weeks of treatment. This gives an opportunity to follow the reticulocyte count, to gage the efficiency of response to treatment and to emphasize to the patient the seriousness of the disease. We have followed the principle of giving 15 units of extract daily for two weeks. A similar amount is prescribed twice a week for the remainder of a three month period. Weekly injections of 15 units are then given for three months, followed by twice monthly injections for six months. After this intensive treatment for one year, injections are given monthly for the remainder of the life of the patient. Usually 15 units are enough; 30 units will supply any need. Once the correct diagnosis of pernicious anemia is made, we know that the patient will always have pernicious anemia. There is no record of a recovery from true addisonian idiopathic pernicious anemia. The disease is not cured; there is only compensation for the deficiency by the administration of sufficient potent liver extract. Treatment must be constant and continuous through the life of the patient.

What results are obtained by adequate and complete therapy? The blood and bone marrow return completely to normal and remain so unless some other disease or factor disturbs the hematopoietic system. A neurologic lesion never develops under adequate and complete liver therapy. Usually a systematic improvement in an existing cord lesion occurs with intensive liver therapy, although the signs of cord involvement, such as absent vibratory sense and altered reflexes, usually persist. Only rarely does a patient remain disabled with proper therapy.

The achlorhydria always continues; the remainder of the gastrointestinal symptoms and signs disappear. The papillae of the tongue return to normal, the glossitis and diarrhea disappear, the body nutrition and absorption from the small intestine proceed normally and indigestion causes no more trouble.

The treatment of this serious disease is so satisfactory with complete liver extract therapy that the patient returns to normal and remains normal with continuous adequate therapy. There is no greater triumph in medicine than the marvelous response of this previously fatal disease to liver therapy.

Folic acid has already been mentioned as a possibly specific chemical substance needed by the bone marrow to complete the growth of red cells. According to this concept, it is actually incorporated into the red cell stroma to assure normal growth. Liver extract does not actually become a part of the cell stroma. Folic acid may cause the blood and marrow to return to normal, although the results are not so constant as with liver therapy. With adequate folic acid therapy the tongue and gastrointestinal tract may also return to normal. It is doubtful that a response on the part of the marrow and gastrointestinal tract is as satisfactory or constant as with liver therapy. In other types of macrocytic anemia, such as with sprue, the results may be even better with folic acid than with liver. The treatment of macrocytic anemias other than addisonian pernicious anemia is, however, another subject.

Folic acid does not influence the neurologic lesion. Many cases have been reported in which cord lesions have developed under folic acid therapy. The statement has been made that two thirds of the patients under folic acid treatment present a spinal cord lesion during adequate therapy. It seems probable that folic acid is in no way related to the cord lesion, but that some unidentified substance made available by liver therapy is the specific principle in the neurologic lesion.

We see no reason for depending on folic acid for the treatment of pernicious anemia. This point is emphasized by all competent observers. Is it of value to add folic acid to liver extract? There is no good evidence to support such a view if the liver therapy is complete. Folic acid only adds to the cost of treatment. With adequate and potent liver extract therapy the results in the treatment of pernicious anemia are so ideal that no change should be made at present.

Should auxiliary treatment be given? We see no reason to prescribe iron, hydrochloric acid, digestive ferments, mineral salts or vitamins. The patient should have a complete wholesome diet with adequate protein. Most patients will have good food intake spontaneously, since the appetite quickly improves and food is taken after adequate liver therapy.

An allergy rarely develops to parenteral liver extract. One can avoid the possibility usually by changing the type of liver extract. The reaction is due to the specific animal and not the liver as such. Since extracts from beef, hog, horse and sheep may be used, the allergy problem can almost always be managed. When the use of liver extracts parenterally is impossible, oral therapy should be tried with or without antihistaminic drugs, such as diphenhydramine hydrochloride ("benadryl hydrochloride") or tripelennamine hydrochloride ("pyrabenzamine hydrochloride"). The reaction from parenteral injections may be prevented by the addition of small amounts of epinephrine.

If all liver therapy is impossible, folic acid may then be used without influencing an existing neurologic lesion. Such a lesion is likely also to develop during adequate folic acid therapy. Some observers have expressed the thought that this development might be more possible with folic acid.

SUMMARY

Addisonian idiopathic pernicious anemia is a deficiency disease affecting the bone marrow, the nervous system and the gastrointestinal tract. This deficiency is responsible for the characteristic macrocytic anemia and megaloblastic bone marrow, the subacute combined sclerosis and peripheral neuritis, the glossitis and other gastrointestinal symptoms. The fundamental defect is in the stomach mucosa, and, once there, is always present.

All manifestations of the disease can be prevented and relieved by proper therapy. Treatment is necessary throughout the life of the patient if the diagnosis is correct. Liver therapy is perfect treatment with proper technic and a potent preparation. More than one substance is deficient, but all absent factors become available with liver therapy. Liver is best given as a potent extract parenterally. Treatment should be intensive at the onset to more than satisfy the deficiency. Treatment must be given regularly and adequately for the life of the patient. Folic acid is only partial therapy and does not relieve the deficiency responsible for the neurologic lesion, which is the most serious aspect of of the disease.

Until the introduction of liver therapy pernicious anemia was invariably fatal. The serious crippling lesion of the disease is involvement of the nervous system. This can be prevented and often helped by liver therapy but not by folic acid. A method for administering liver extract which has proved highly satisfactory for a large number of patients is outlined.

ABSTRACT OF DISCUSSION

DR. FRANK H. BETHELL, Ann Arbor, Mich.: I agree with the speaker that no treatment other than with refined liver extract is ordinarily needed for pernicious anemia. Crude extracts have no advantages over the refined and concentrated types. Vitamins have no value except to relieve deficiency. I am not prepared to accept fifteen units per month as adequate treatment for the majority of patients with pernicious anemia. We have found that fifteen units twice a month is perhaps a safer dose, particularly since there are no ill effects from giving more treatment than is required. A careful hematologic examination is the only way one can measure the adequacy of maintenance therapy. It does not do to wait for the return of symptoms. A careful hematologic examination includes a determination of erythrocyte size by means either of diameter measurement or estimation of mean corpuscular volume. Unless cell size is within normal limits, the treatment cannot be said to be adequate. Folic acid, as Dr. Haden mentioned, has a distinctly limited field in the treatment of pernicious anemia; indeed, it is questionable whether it should ever be employed. It is about equally effective by both oral and parenteral routes of administration. Combinations of liver extract and folic acid are irrational, because of the different dose requirements and different excretion rates of the two substances. Folic acid should never be given to patients with evidence of nervous system disease, and others receiving it should be kept under close observation for development of neurologic manifestations. If such appear, folic acid therapy should be discontinued immediately and liver extract substituted for it. The recent announcement of a crystalline substance isolated from liver and tentatively named vitamin B_{12} may lead to complete revision of the specific treatment of pernicious anemia and related macrocytic anemias. This compound in our hands at Ann Arbor has induced optimal hemopoietic responses in patients with pernicious anemia in doses as small as 1 mg. daily. As the speaker indicated, medicinal iron preparations are not ordinarily valuable in the treatment of pernicious anemia. However, when hypochromia or a low color index is present after response to

specific therapy, ferrous salts should be prescribed in divided daily doses of 1 to 2 Gm. Most female patients with pernicious anemia before the menopause benefit from the adjunct use of medicinal iron. Hydrochloric acid occasionally has a place in treatment, at least temporarily. A dose of 2 to 4 cc of the U. S. P. dilute solution given in water with meals may have a beneficial effect on digestion and aid in controlling diarrhea, especially in the early period of treatment. It has no specific value, and it usually can be discontinued without recurrence of digestive symptoms after remission is well established.

DR. HOWARD L. ALT, Chicago: The considerable literature on the effect of folic acid in pernicious anemia has led to some confusion as to how this disease should be treated. For this reason, the paper of Drs. Haden and Bortz is timely in pointing out clearly the treatment of choice in pernicious anemia. Folic acid has been relegated to a rather insignificant place in treatment. My co-workers and I have not used intensive parenteral liver therapy for the period of time advocated by Dr. Haden. It has been our custom to give about 150 units of liver the first week and then 15 units once a week until the blood picture is normal and the cord symptoms and signs become static. In our experience, relapses are not uncommon with the parenteral administration of 15 units of liver once a month. On the other hand, 30 units every twenty-one days will maintain the disease in practically all cases in complete remission. I am glad that Dr. Haden pointed out the difference in potency of 15 unit liver preparations manufactured by different companies. It is wise to use a single preparation in order to know what that one will do. In maintaining patients in complete remission, a careful study of the symptoms, physical signs and the blood picture should be made every three or four months. We have found it useful to tabulate neural symptoms and signs, including a record as to whether the vibration sense is normal, diminished or absent from the iliac crests to the malleoli. A decreasing vibration sense is a sign of inadequate treatment. As the authors said, liver extract therapy completely controls the deficiency in pernicious anemia and cannot be replaced by folic acid therapy, which only partly controls the deficiency.

DR. HYMAN I. GOLDSTEIN, Camden, N. J.: In *The Review of Gastroenterology* (**9**:406-411 [Nov.-Dec.] 1942) I published an article, "Pernicious Anemia Alternating with Polycythemia (Polyglobulia)," and cited some cases of pernicious anemia in which a polycythemic response occurred during liver therapy. Has Dr. Haden met with such cases? Free hydrochloric acid was never noted in these cases. Dr. Haden decries the use of folic acid and (oral) hydrochloric acid and recommends the use of liberal parenteral doses of liver extract. Most of us are in accord with everything he propounded today. May I call attention to the early use of liver therapy in anemia by Paul Carnot, Maurice Perrin, of France, P. F. Castellino (1864-1933) and Alfonso Pirera (born Feb. 16, 1877) of Naples? Pirera fed dogs and rabbits liver (after they had been bled) and gave them injections of liver extract and liver juice (1910-1912). Perrin used liver and noted the improvement in the blood in patients with "alcoholic cirrhosis of the liver" (1904, 1905, 1908). Pirera (Tommasi **7**:601-617 and 625-636, 1912) noted that granulocytes were increased by liver therapy. In 1934, Murphy suggested the use of liver in granulocytopenia. James S. Combe (Tr. Med.-chir. Soc. Edinburgh **1**:194-204, 1824) reported a case of pernicious "idiopathic" anemia with necropsy long before Thomas Addison; and P. F. A. Marquis in 1846 wrote on "De l'influence de l'anémie sur le système nerveux," (Thesis, Paris, No. 1, 1846). No mention is made of the reports by E. Geddings (Baltimore M. & S. J. **2**:325-366, 1834) and "F.," a physician of Rhode Island (A Dissertation on Anemia, Boston M. & S. J. **20**: 101-108, 117-124 and 133-138, 1839). It is unfortunate that we are such poor linguists and so have overlooked and delayed the use of liver therapy in anemia for twenty or twenty-five years until the epoch-making article on liver feeding by Minot and Murphy appeared in THE JOURNAL August 14, 1926.

DR. WILLIAM P. MURPHY, Boston: Through almost twenty-five years of experience in the treatment of pernicious anemia my colleagues and I have become convinced that it is one of the few diseases which can be treated entirely on a quantitative basis. There are few diseases in medicine which can be so treated, and it is up to us as individuals and also as a profession not to fumble the ball at this time, failing to treat our patients adequately or properly. Two circumstances make it possible and desirable to treat pernicious anemia on a quantitative basis. We have in this country liver extracts which are well standardized and well prepared. Unfortunately, there are few countries other than this where liver extracts are standardized. We also have available a simple and readily utilizable means of following the effect of treatment to determine whether or not it is adequate. In regard to liver extracts, I again wish to emphasize that the treatment of choice is by the parenteral route and with those extracts which are the most highly potent and refined rather than with the so-called crude extracts. A crude extract means simply that there are inert substances left in it which have no value in the treatment of pernicious anemia. One might say that it is crude therapy and not crude extract that we use at times. With the 15 unit, 1 cc. material, as a unit or basis for treatment, it has been our custom to give as initial treatment rather large doses. Thereafter we give 15 units each week, following the hemoglobin and erythrocyte levels at intervals of one to two months; as the levels reach or rise above normal, the interval between injections is increased. That is, we do not change the size of the dose, for I believe that there are certain objections to that in some patients, but we increase the interval between the dose up to two, three or four weeks, depending on the indications from the blood picture. This treatment is again followed for a period of months, during which time we check the blood at three month intervals. If the tendency is for the erythrocyte level to rise above the 5,000,000 mark, the interval between injections is increased; if the erythrocyte levels are falling during the sequence of counts, the interval between injections is shortened. In this way the blood levels are constantly under observation, making it possible for one to increase or decrease the intake of antipernicious anemia substance according to the need of each patient. Regulation of the dosage in this way, we believe, is the best assurance of an adequate supply of liver extract to prevent or to improve the difficulties which may result from spinal cord damage and to avoid the expense and inconvenience of overdosage. Some patients need injections of 15 units each week. A few need it oftener than that. Some of our patients are maintained with normal blood levels and with no complications produced by pernicious anemia with injections as infrequently as every four, six or eight weeks.

DR. RUSSELL L. HADEN: If more than 15 units of liver extract is needed monthly we prefer to give a single injection of 30 units. This method works just as well, and the patient likes it better. It is most important to have a periodic check of the blood to determine the efficacy of treatment, as Dr. Murphy has emphasized. The treatment should be so regulated that the red cell count never fails. The first change in the blood if treatment is not complete is an increase in the size of the red cell best indicated by the volume index, so that we follow the volume index closely. The tongue is an excellent indicator also of the completeness of treatment. If the need for liver extract is not completely satisfied the characteristic clean smooth tongue of active disease quickly appears. The condition of the tongue should always be carefully observed. The question was brought up whether the red cell count will rise too high if an excessive amount of liver extract is given. Rarely a patient may have both pernicious anemia and idiopathic polycythemia vera. When liver extract is given during the pernicious anemia phase, the polycythemia vera becomes active and the red cell count becomes very high. We have one such patient under observation now. Dr. Goldstein raises the question of who was responsible for liver therapy. Dr. Osler long ago emphasized that the credit for a discovery in medicine should go to the person who convinced the world and not to the person to whom the idea first occurred. Dr. George Minot and Dr. William Murphy were the discoverers of the value of liver in the treatment of pernicious anemia.

CARONAMIDE AND PENICILLIN

Serum Levels in Human Beings, Following Multiple Doses of the Drugs

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Numerous attempts have been made to increase the efficacy of penicillin in the treatment of infections by altering the rate of its absorption or excretion. Beyer and his associates have reported that caronamide (4'-carboxyphenylmethanesulfonanilide), though excreted only by the glomeruli, alters the specific renal tubular enzyme system responsible for the excretion of penicillin.[1] The excretion of penicillin is delayed, so that a higher concentration may be maintained in the blood for more prolonged periods. Other investigators have confirmed the original reports on the penicillin-enhancing effect of caronamide and have noted that the drug is relatively nontoxic when administered over short periods of time.[2]

There is difference of opinion concerning the dose of caronamide necessary to maintain an effective concentration of penicillin in the blood. Direct information on the absorption and excretion of caronamide in human beings has been lacking, since practical methods of measuring the concentrations of the drug in the blood and urine have not been available until recently. Furthermore, the effects of the drug have been studied only during short courses or single interval periods of administration. If the drug has a cumulative effect, concentrations in the blood which might lead to dangerous toxic reactions could easily be produced during more prolonged courses.

The following study was undertaken in an effort to compare the effect of different doses of caronamide on the serum levels of penicillin and caronamide in human beings while the drugs were being administered simultaneously during a three day period.

MATERIALS AND METHODS

The 17 subjects used in this study were ambulatory convalescent patients at the North Carolina Baptist Hospital. All were under the age of 60, and none showed evidence of impaired cardiac, renal or hepatic function. The concentrating power of the renal tubules, as measured by the specific gravity of the urine in all patients and by the phenolsulfonphthalein excretion test in 10 patients, was within normal limits. Diet, salt and fluid intake were unrestricted. No medication was given during the test period which might affect the determination of the serum levels of penicillin and caronamide or interfere with the excretion of the drugs.

One hundred thousand units of commercial crystalline penicillin G[3] was given intramuscularly every four hours day and night for seven days. On the second, third and fourth days, caronamide[4] was simultaneously administered orally to 7 patients (group A), in doses of 2 Gm. every four hours day and night, and to 10 patients (5 each in groups B and C), in doses of 4 Gm. every four hours day and night. The intervals were arranged so that the drugs were always given one-half to one hour before meals to insure better absorption of the caronamide. One to three blood samples were taken daily on the first through the fourth days and on the seventh day. In groups A and B the samples were taken four hours after administration of the drugs and in group C two hours after administration. Serum was removed aseptically and stored at —20 C. Determinations of the penicillin and caronamide levels were then carried out by groups to minimize the technical variations.

Penicillin levels were determined by the dilution method. Serums were diluted serially in 0.5 cc. of tryptic digest beef heart broth, and 50,000 to 100,000 organisms from an eighteen to twenty-four hour culture of beta hemolytic streptococci (strain NY 5) were used as a reference inoculum; this inoculum is inhibited by 0.008 unit of penicillin per cubic centimeter, so that a minimum serum level of 0.0156 unit per cubic centimeter (charted as 0.02) can be measured. The tubes were inspected after 18 hours' incubation at 37 C., and in all cases the result was checked by streaking the broth on a segment of a blood agar plate. The end point was considered the tube in which no growth occurred; if a tube showed no visible growth, but a few colonies appeared on the blood agar streak, the value was recorded midway between that tube and the next tube showing no growth.

Levels of caronamide in the serum were determined by the method of Ziegler and Sprague, which utilizes the Evelyn photoelectric colorimeter.[5] Eighty to 90 per cent of the total caronamide is recovered by this procedure, but the amounts of bound and free drug are not differentiated. A small percentage of the colorimetric value is made up of unidentified metabolic products of caronamide.[1c]

RESULTS

Effect of Doses of Two Grams of Caronamide on Penicillin Level Four Hours After Administration (Group A).—The effect of 2 Gm. of caronamide, given orally every four hours, on the level of penicillin in the serum four hours after an intramuscularly administered dose of 100,000 units (group A) is shown in figure 1. The average of all determinations of penicillin in the serum in the group (indicated by a solid line in the chart) was 0.06 unit per cubic centimeter on the first day and 0.09 unit per cubic centimeter on the seventh day—the control periods before and after caronamide therapy, respectively. On the second day of the test—the day simultaneous caronamide and penicillin therapy was begun—the average was 0.1 unit per cubic centimeter; on the two successive days the average was 0.17 and 0.14 unit per cubic centimeter.

Moderate variations in concentrations of penicillin in the serum were observed in individual patients in group A during all phases of the test period. Three out of the 7 patients showed no significant effect from the administration of caronamide at any time; in the remaining 4, intermittent twofold to fourfold increases in the level of penicillin in the serum were observed on six occasions. In these subjects the rises occurred

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Dr. Meads is a Markle Scholar in Medicine.

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From the Department of Internal Medicine, Bowman Gray School of Medicine of Wake Forest College and the North Carolina Baptist Hospital, Winston-Salem.

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3. The penicillin used in this study was supplied by Wyeth, Inc., Philadelphia.

4. Sharpe and Dohme, Inc., Philadelphia, furnished the caronamide used in this study. Dr. William P. Boger, associate medical director, made available to us the results of several of his studies prior to their publication.

5. Ziegler, C., and Sprague, J. M.: A Colorimetric Determination of Caronamide, J. Lab. & Clin. Med. **33**: 96-100 (Jan.) 1948.

during the third or fourth days, after two or three days of combined therapy; in 5 of the 6 instances they were followed later in the same day by levels similar to those observed during the control periods before and after caronamide therapy.

Effect of Doses of Four Grams of Caronamide on Penicillin Level Four Hours After Administration (Group B).—The effect of 4 Gm. of caronamide, given orally every four hours, on the level of penicillin in the serum four hours after an intramuscularly administered dose of 100,000 units of penicillin (group B) is shown in figure 2. The average of all determinations of penicillin in the serum in the group was 0.065 unit per cubic centimeter on the first day and 0.04 unit per cubic centimeter on the seventh day. On the second day of the test the average level of penicillin in the serum was 0.063 unit per cubic centimeter; on the two succeeding days the average was 0.25 and 0.26 unit per cubic centimeter.

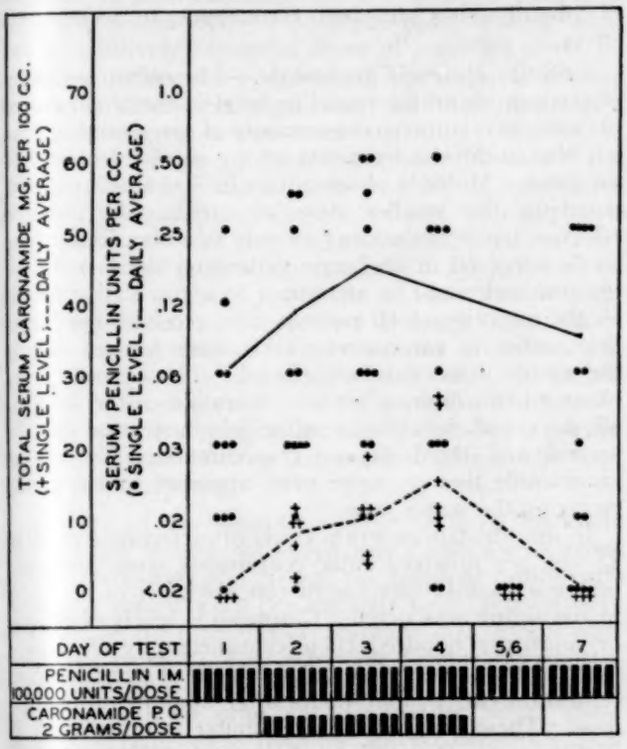

Fig. 1.—Effect of 2 Gm. of caronamide, given orally every four hours, on the serum level of penicillin four hours after an intramuscularly administered dose of 100,000 units of penicillin. (Group A.)

As with the lower dosage of caronamide (group A), variations in penicillin levels in the same patient and between patients in the group during the seven days of observation were moderately wide. Each of the 5 subjects showed at least one significant elevation in the concentration of penicillin in the serum; nine of the twelve significantly increased titers were observed in 2 patients. In these 2 patients the rises in titer were noted on four and five consecutive determinations, respectively, suggesting a sustained elevation in concentration. One of eleven samples taken on the second day showed a twofold rise in penicillin titer. On the third day six of ten samples showed a twofold to fourfold increase, and on the fourth day five of eight samples revealed a twofold to eightfold increase. Samples taken during the test period before the elevations occurred and after they subsided showed levels no greater than those obtained during the control periods before and after caronamide therapy.

Effect of Doses of Four Grams of Caronamide on Penicillin Level Two Hours After Administration (Group C).—The effect of 4 Gm. of caronamide, given orally every four hours, on the levels of penicillin in the serum two hours after an intramuscularly administered dose of 100,000 units of penicillin (group C) is shown in figure 3. The enhancing effect of caronamide on penicillin concentrations is more pronounced at this interval than at four hours. The average of all determinations of penicillin in the serum in the group was 0.08 unit per cubic centimeter on the first day and 0.05 unit per cubic centimeter on the seventh day. On the second day of the test the average level of penicillin in the serum was 0.57 unit per cubic centimeter; on the two succeeding days the average was 1.25 units per cubic centimeter and 1.06 units per cubic centimeter.

The effect of caronamide on penicillin levels two hours after administration was fairly consistent in each subject, but varied widely among the 5 subjects in the group. During the second day of therapy, ten of eleven blood samples showed a threefold to eightfold increase in penicillin concentration. The maximum effect was reached the following day; each of eleven samples had a fourfold to seventeenfold increase. On the fourth day, the penicillin concentration was slightly lower, though nine of ten samples showed a fourfold to thirteenfold rise in titer.

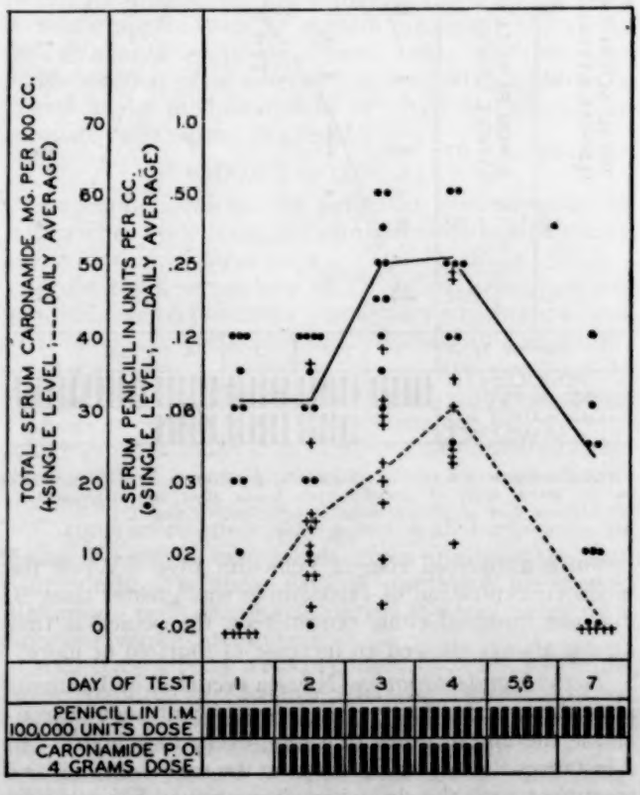

Fig. 2.—Effect of 4 Gm. of caronamide, given orally every four hours, on the serum level of penicillin four hours after an intramuscularly administered dose of 100,000 units of penicillin. (Group B.)

Serum Levels of Caronamide.—The levels of caronamide in the serum in groups A, B and C are plotted on figures 1, 2 and 3, respectively. The trends and variations closely parallel those for penicillin. The average concentrations (indicated by broken lines in the charts) rose progressively during the three days of caronamide

therapy in all groups. With a dose of 2 Gm. every four hours, the average levels of caronamide in the serum four hours after administration (group A) were 7.8, 9.5 and 16.1 mg. per hundred cubic centimeters on the second, third and fourth days, respectively. With 4 Gm. every four hours, the levels of caronamide in the serum four hours after administration (group B) averaged 14.0, 21.7 and 30.3 mg. per hundred cubic centimeters on the second, third and fourth days. With a dose of 4 Gm., blood samples taken two hours after administration (group C) on these days showed average caronamide levels of 25.3, 38.6 and 46.2 mg. per hundred cubic centimeters.

The penicillin concentrations reached a peak on the third day and then leveled off. In the great majority of instances, a level of caronamide in the serum of 20 to 25 mg. per hundred cubic centimeters was necessary to

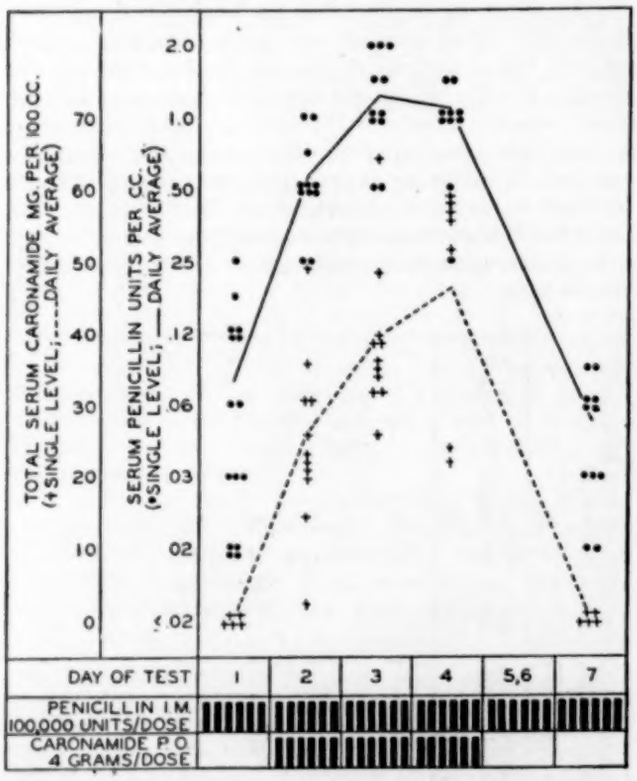

Fig. 3.—Effect of 4 Gm. of caronamide, given orally every four hours, on the serum level of penicillin two hours after an intramuscularly administered dose of 100,000 units of penicillin. (Group C.)

produce a twofold rise in penicillin titer. When the blood concentration of caronamide was greater than 30 mg. per hundred cubic centimeters, the penicillin titer almost always showed an increase of fourfold or more.

Toxic Manifestations.—Nausea occurred in 3 patients after thirty-six to forty-eight hours of continuous caronamide therapy in doses of 4 Gm. every four hours. In 2 instances the nausea occurred in the early morning and treatment with the drug was discontinued before blood samples were taken. In the third, nausea developed when the caronamide levels four hours after administration of a dose were 47 and 50 mg. per hundred cubic centimeters. Two patients had no complaints with caronamide levels of 50 and 60 mg. per hundred cubic centimeters two hours after administration of a dose. One patient vomited soon after receiving a dose of caronamide.

COMMENT

The results of this study indicate that caronamide has a cumulative effect when administered over a period of three days in doses similar to those which have been used by previous investigators during shorter intervals. The potentially toxic effects of caronamide suggested by these experiments call for a reevaluation of the use of the drug. The benefits achieved by raising the blood levels of penicillin must be balanced against the dangers of administering sufficient caronamide to secure this effect.

Effective Dose of Caronamide.—The enhancing effect of caronamide on the penicillin level in the blood varied not only in relation to the amounts of caronamide given, but also in different patients taking similar amounts of the drug. Multiple observations in 3 of the 7 patients receiving the smaller dose of caronamide revealed effective levels of the drug on only two occasions; these levels occurred in the same patient on the last day of the test and could be attributed to a cumulative effect. In the majority of 10 patients who received the larger dose, effective caronamide levels were present during the entire three day test period. These levels were observed two hours after administration of the drug on all days and four hours after administration on the second and third days. The cumulative effects of caronamide therapy were most apparent in the group receiving the larger dose.

In most instances serum levels of caronamide of 20 to 25 mg. per hundred cubic centimeters were necessary before a twofold increase in concentration of penicillin in the serum was noted. Caronamide levels of 30 mg. or more per hundred cubic centimeters resulted in a fourfold to seventeenfold enhancement of penicillin concentration two to four hours after administration of a dose. These observations are similar to those made in 2 patients by Boger, Kay, Eisman and Yoeman, who observed that 20 to 30 mg. of caronamide per hundred cubic centimeters of serum were required to inhibit the excretion of penicillin by normal renal tubules.[6]

It would, therefore, appear that caronamide levels approximating 30 mg. per hundred cubic centimeters of serum are necessary for an effective increase in levels of penicillin in the serum. Beyer and his associates have observed in dogs that a uniform blood level of caronamide is readily achieved by a large initial dose of the drug, followed by a smaller maintenance dose.[1b] It would appear that a similar dosage schedule is indicated in human beings to maintain an effective serum concentration of caronamide without the dangers of cumulative effects.

Seeler, Wilcox and Finland [2a] observed that relatively low doses of caronamide are effective in enhancing serum levels of penicillin in patients more than 60 years old. They suggest that the decreased tubular mass commonly present in aged persons is responsible for this.

Application to Penicillin Therapy.—In view of the demonstrated effectiveness of caronamide in raising serum levels of penicillin, the drug would appear to be a useful adjunct in the treatment of certain types of infection, provided that its potential dangers are not too great. In most infections caused by penicillin-susceptible organisms effective levels of the antibiotic are readily attained. Whether caronamide will be found

6. Boger, W. P.; Kay, C. F.; Eisman, S. H., and Yoeman, E. E.: Caronamide, a Compound That Inhibits Penicillin Excretion by the Renal Tubules, Applied to the Treatment of Subacute Bacterial Endocarditis, Am. J. M. Sc. **214**: 493-502 (Nov.) 1947.

to have a place in the treatment of such infections is an economic question that will depend on the eventual cost of caronamide and penicillin. In some infections due to susceptible organisms effective serum levels can not be attained economically with penicillin alone. An example of such an infection would be a localizing abscess, where higher serum levels are necessary to penetrate a relatively avascular or necrotic inflammatory barrier. In such cases caronamide would be useful in achieving serum levels of penicillin not attainable without prohibitively expensive doses of penicillin alone.

Infections due to organisms of low susceptibility or to usually susceptible organisms which have acquired a moderate degree of resistance sometimes respond to high concentration of penicillin in the blood stream. Effective levels can occasionally be achieved by massive doses of penicillin, and this method has been employed in cases of subacute bacterial endocarditis due to relatively resistant strains of organisms. Penicillin alone is a drug of low toxicity, even in massive doses. Additional experiments are necessary before a definite conclusion can be reached as to the value of caronamide given over a long period in such infections. The higher and more effective serum levels of penicillin which could be achieved thereby might decrease the tendency toward the development of drug fastness and shorten the total course of the illness.

Toxicity of Caronamide.—Three of the 17 patients in this study became nauseated, and 1 vomited. Caronamide levels of 47 and 50 mg. per hundred cubic centimeters of serum were present four hours after a dose of 4 Gm. on the third day of treatment in 1 subject with persistent nausea. This symptom disappeared shortly after caronamide therapy was stopped. Unfortunately, treatment with the drug was discontinued before blood samples were obtained from the other 2 patients. This single observation suggests that in some persons the range between effective and toxic serum levels of caronamide may limit the usefulness of the drug. Strauss and his associates observed mild gastrointestinal disturbances in patients who were receiving caronamide, penicillin and sodium benzoate orally over a period of twenty-four hours.[2b] They were unable to determine which drug was responsible for these symptoms.

Evidence of renal damage during the administration of caronamide was observed by Boger and his associates in 1 patient; in view of the time relationship, this damage may have resulted from cumulative caronamide serum levels.[6] This patient was receiving 3 Gm. of caronamide every three hours; on the eighth day of continuous administration, red and white cells appeared in the urine, accompanied with a slight rise in blood urea nitrogen and a decided drop in urea clearance. These abnormalities disappeared within a few days after caronamide therapy was discontinued.

The drug is similar in chemical structure to compounds of the sulfonamide group, which are known to cause toxic effects. Boger records Duncan's observation of a rash which was probably due to caronamide. One of us (G. T. H.) has seen a patient in another hospital who showed red and white cells in the urine, as well as nodules in the skin and subcutaneous tissues, painful hyperemic swelling of the interphalangeal joints and scaling of the skin. These observations suggest that caronamide like the sulfonamide drugs may produce changes similar to periarteritis nodosa.

Animal experiments on the toxicity of caronamide given over long periods are reported by Beyer and his associates.[7] Six dogs received caronamide in oral doses ranging from 0.4 to 1.5 Gm. per kilogram of body weight for a four week period. No consistent effect on the amounts of creatinine, urea and nonprotein nitrogen in the blood or on the content of creatinine, urea nitrogen and total nitrogen in the urine was noted. At the end of the test period no abnormal microscopic changes were observed in renal sections. The experimental conditions were optimal for preventing renal damage and limiting drug accumulation. Young dogs were used; the test diet produced a relatively alkaline urine, and the high fluid intake resulted in a large daily output of urine with a low specific gravity.

Studies on human subjects over short periods of time have revealed no definite symptoms or laboratory observations suggestive of renal damage. Children given caronamide over a period of one or two weeks in daily doses of 0.1 to 0.4 Gm. per kilogram of body weight showed no definite toxic effects.[2a] Longer periods of study in human beings are necessary for final evaluation of the potential toxicity of caronamide.

NEED FOR PHARMACOLOGIC STUDIES IN HUMAN BEINGS

Most studies on caronamide in human beings have been based on a single dose or on the administration of the drug over a period of twenty-four hours or less. Long term studies employing doses of 3 Gm. every three hours or 4 Gm. every four hours, as are being recommended, are urgently needed.

Caution should be urged in the use of the drug pending further evaluation by many investigators. At present it would appear wise to control treatment by testing the caronamide level once or twice a day, two hours after administration of a dose of the drug. In addition, a liberal intake of fluid should be given to maintain an adequate daily output of urine.[8]

SUMMARY AND CONCLUSIONS

Caronamide raises the penicillin concentration in serum when both drugs are administered simultaneously over a period of three days.

Ordinarily a serum level of 25 mg. of caronamide per hundred cubic centimeters is necessary to achieve a twofold increase in penicillin concentration in the serum; caronamide levels exceeding 30 mg. are necessary to increase the penicillin concentration fourfold or more.

Doses of 4 Gm. every four hours are necessary to achieve a caronamide level of 30 mg. per hundred cubic centimeters of serum four hours after the oral administration of the drug.

A cumulative effect was noted with both doses of 2 and 4 Gm. of caronamide given orally every four hours during the three days of continuous treatment. Maximum penicillin levels were achieved after two days of combined treatment

Mild toxic effects were produced by levels of caronamide required to achieve effective enhancement of penicillin concentrations in the serum; other writers have noted severer reactions.

Caronamide should be used with caution until long term pharmacologic studies in human beings are completed. Until this time it is strongly suggested that the blood level of caronamide be followed and adequate urinary output maintained during treatment, particularly in cases in which decreased renal function is suspected.

7. Beyer, K. H.; McKinney, S. E.; Tillson, E. K., and Green, C. W.: 4'Carboxyphenylmethanesulfonanilide (Caronamide): Its Toxicologic Effects, J. Pharmacol. & Exper. Therap. **91**: 263-271 (Nov.) 1947.

8. Earle, D. P., Jr., and Brodie, B. B.: The Renal Excretion of 4'-Carboxyphenylmethanesulfonanilide (Caronamide), J. Pharmacol. & Exper. Therap. **91**: 250-254 (Nov.) 1947.

WHAT IS PSYCHOTHERAPY TO THE INTERNIST?

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Study and treatment of the patient as a whole implies a psychologic as well as an organic approach and requires the combined endeavor of clinicians and psychiatrists. Many internists carelessly or by design develop a technic which obviates grappling with the patients' psyche. One group emphasizes the importance of the subtle art of physical diagnosis and spotlights the discovery of a faint diastolic murmur or the tip of a palpable spleen, while a second group divert themselves and each other by a complicated study of the chemical dislocations of various syndromes. A third group specializes in every available drug and synthetic preparation, and to this group each symptom or threat of a symptom calls for a therapeutic order. To all of these groups the business of ministering to the psychologic aspects of disease is someone else's obligation. If the patient is neurotic, let him be sent to physicians who specialize in neurosis. I suspect that the physicians in these three groups, and there are other similar groups, unconsciously, at an early stage, began to avoid involvement in the complex and illusive aspects of human nature. They are inept when dealing with personalities and therefore tend to consider psychiatrists unnecessary except for psychotic patients. They inveigh against the tendency to invite psychiatrists in to the study of cases before all organic disease has been eliminated. Some of them think that psychoanalysis is inadequately substantiated. Others believe that analysts, when they delve into the personality structure, using the theoretical concept of symbolism of the unconscious, will find abnormalities in every person which they will attempt to rearrange into a "normal" pattern.

Perhaps I have said enough to give an inkling of the tremendous prejudice I have noticed throughout the medical profession against admitting formal psychologic or psychiatric approach to all medical patients. I shall not belabor the point further nor attempt to defend or condone psychiatry or psychosomatic medicine. What I shall try to do is to clarify the significance of the straws that are blowing past in ever increasing numbers in the stiff breeze of scientific study of the psychologic aspects of organic disease.

In former years the psychology of medicine was learned only by observing how experienced clinicians handled sick human beings. This aspect of the care of patients came to be distrusted in the time of Osler, Shattuck, Delafield and the other leaders of the systematic study of medicine. They became preoccupied with developing and improving accurate diagnosis. The zealous search after etiologic factors, coupled with the discovery that many of the time-honored drugs in the pharmacopeia were inert, inevitably concentrated attention on treatment in those cases in which diagnosis could be substantiated and therapeutic results could be accurately measured. The power of suggestion by placeboes was recognized, but was utilized mainly as a control in studies of drug therapy.

During this period psychiatry, independently, was making great progress, although in most instances it was isolated in mental institutions which were far away from hospitals for medical and surgical cases. As it became apparent that many medical cases had important psychologic aspects as well, the psychiatrists were consulted. Appel,[1] writing about psychiatric therapy, stated:

> When a patient comes to the doctor he is in an attitude of expecting relief not only from his physical symptoms but from his insecurity. It is important for the physician to be aware of this psychological tradition even if he is treating an organic illness, and to use suggestion constructively and not destructively. It is here that the physician's manner and bearing are so important. Indefiniteness, lack of assurance, uncertainty, undue gravity, or silence may be devastating to the patient. Such behavior feeds his imagination and apprehension with all sorts of forebodings. A hasty word or an incomplete explanation may leave the patient with almost unbearable insecurity or fright.

The introduction of psychiatric thinking into medical problems soon uncovered a wide field, the exploration of which has come to be known as psychosomatic medicine. This departure from the orthodox concept of internal medicine has not been easily accepted. It is confused by some with that part of the psychologic approach to patients which seemed to be well handled by our grandfather general practitioners but has been lost sight of by the specialists of today. To others the psychiatric explanation of common symptoms still sounds strange. For instance, Saul[2] discussed hunger pains as follows:

> In the gastric ulcer cases the impulses involved are apparently less various, and consist more specifically of frustrated desires for love, care, dependence and the like. These have become so intimately associated with the functioning of the stomach that cravings for them cause the stomach to behave physiologically just as though they were expecting food.

This is difficult for many physicians to agree to without reservation or to consider as fundamentally important from an etiologic point of view.

With recognition of this strong antagonism to the application of anything even suggestive of a freudian approach to somatic problems there still is much general interest in the rapidly growing mass of evidence which tends to show the functionally intimate interrelationship between psyche and soma, mind and body, the consciousness, on the one hand, and needs, urges, responses to the environment (especially parental behavior) on the other.[2a] As internists we should encourage the correlated studies of emotions and bodily changes, but meanwhile we must recognize that, like it or not, we are implicated in our patient's emotional reactions to disease and must apply ourselves to this problem. Before the days of Lister it was no mistake to put dirty hands into a wound. Today such a blunder would not be countenanced by a trained nurse or medical student. Today we must avoid comparable breaks in technic of psychotherapy.

ILLUSTRATIVE CASES

The following cases illustrate breaks in technic which happen every day. The physician, as Kanner[3] said, "means no harm."

CASE 1.—A 27 year old man had been known to have congenital cardiac disease from infancy. His parents, with good medical advice, had brought him up to take part in all games

Read before the Section on Internal Medicine at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948.

1. Appel, K. E.: Psychiatric Therapy, in Hunt, J. M.: Personality and the Behavior Disorders, New York, The Ronald Press Company, 1944, vol. 1.
2. Saul, L. J.: Physiological Effects of Emotional Tension, in Hunt, J. M.: Personality and the Behavior Disorders, New York, The Ronald Press Company, 1944, vol. 1.
2a. Cobb, S.: Borderlands of Psychiatry, Cambridge, Mass., Harvard University Press, 1943.
3. Kanner, L.: In Defense of Mothers, New York, Dodd, Mead & Company, Inc., 1941.

and athletic activities that his associates indulged in, and he had played on his high school baseball team. After college he had gone into farming, with hunting long hours in field and forest as his major relaxation. From time to time he had been carefully examined and always had accepted the advice for moderate caution that wise physicians had given him. Recently, he had grippe with high temperature, tachycardia, headache and general malaise. The local physician was called and treated him. Two days later, his temperature having fallen to normal and his general condition having become greatly improved, the local physician casually said to the patient, "I surely am glad you are better. I never saw a worse heart than yours was two days ago." From that time on he became heart conscious, aware of extrasystoles and bothered by faintness and palpitation. He limited his activities and lost much of his former *joie de vivre*. His local physician had planted ineradicably the seeds of worry and fear in this courageous young man's imagination and, in fact, changed his entire life.

CASE 2.—A woman of 44 consulted a physician for a minor ailment. During the checkover her blood pressure was observed to be 220 systolic and 130 diastolic. The physician clearly showed his amazement by his questioning of the patient when he said, "Don't you ever have severe headaches? Aren't you conscious of your heart pounding? Don't you ever get dizzy? Don't you ever get short of breath?" And finally, "Well, you certainly should have some or all of those symptoms with that blood pressure." From then on she became anxious about her health for the first time, and began to experience some of the symptoms her physician had called to her attention.

Comment.—In these 2 cases the symptoms became apparent to the patient directly following ill considered remarks of the physician which resulted in anxious concern and depression. The power that even their lightly spoken words have to instil fear into the minds of patients often is overlooked by physicians. A veritable chain reaction may be set in motion. To an imaginative timid person high blood pressure quickly leads to thoughts of apoplexy, paralysis and death. A cardiac murmur means heart trouble and impending sudden death. In this day of popular medical education in magazines and newspapers, the man on the street always has preconceived notions of cause and effect and of the dangers of most diseases. Therefore, it becomes necessary for the physician to be aware of all the little or big ideas that may act as entering wedges for fear into the patient's consciousness and avoid them or neutralize them on the spot. If the physical examination is discussed in the presence of the patient, abnormalities should be described in technical terms and should be cleared of alarming implications. We all see patients who tell us, "three doctors have warned me that I might have a stroke any minute" or "two doctors have said I might have a sudden heart attack." Actually what these doctors probably told their patients was that they did have some elevation of blood pressure or that there was something wrong with their hearts. What they did not see was the importance of convincing the patient that these conditions in most instances have little or no immediate danger and that what danger they hold may not be encountered for a long time or possibly not until the end of a normal span of years.

The following brief case history illustrates the gravity of misinterpreting the functional aspects of a case.

CASE 3.—A 43 year old man was admitted with the complaint of a gastric ulcer, from which he was supposed to have had hemorrhages within the past two weeks. A year previously, on consulting a physician, he complained of hunger pains and acid eructation. He was told that he had ulcers and was put to bed for four weeks, limited to a milk and cream diet and given blunting powders. For a year thereafter he was kept on a meat-free soft diet, with greatly restricted activities, which precluded work. During this time he lost 25 pounds (11 Kg.). On admission to the hospital he refused to take anything but liquids and lay on his bed deeply depressed and constant in his complaints of abdominal pain. On several occasions he insisted that he had spit up blood from his stomach, although examination of gastric contents and six examinations of the stool, showed no blood. Roentgen and fluoroscopic examination did not reveal any organic lesion or scar, although pylorospasm and hyperacidity were present.

Comment.—The handling of this case demonstrates several of the most distressing results of breaks in therapeutic technic. The treatment itself convinced the patient of the alarming seriousness of the lesion in the stomach, which was a completely erroneous impression. The illness was permitted to drag on with ever increasing fixation of the conditioned invalidism, and the underlying nervous instability received no direct or indirect therapeutic consideration.

PSYCHOLOGIC FACTORS IN ORGANIC DISEASE

In order to avoid contributing to patients' anxiety over their illness and to allay their symptom-producing fears, one must be conversant with the mental aspects of numerous medical conditions. Many of these were brought into sharp focus during World War II. Neurocirculatory asthenia is no longer considered primarily cardiovascular in origin. Mucous colitis is more a symptom than a disease. Gastric ulcer is coming to be regarded by many as an organic complication of an underlying neurosis [4]; cardiospasm and pylorospasm are of the same type. The important possibility of a major role being played by psychic disorders in the causation of certain types of hypertension and of exophthalmic goiter [5] is recognized. Angina pectoris, allergic diseases, many forms of dermatitis, migraine, glaucoma and obesity—all are now known to be tremendously aggravated by nervous tension and anxiety. Too little attention has been paid to worry, anxiety and depression engendered by disease itself, since the best treatment of these mental states is the prompt and efficient correction of the underlying disease.

Although many able physicians make no effort to understand the psychologic implications of organic disease, some of the more sensitive ones tend to "soften the blow" too much, even to the point of deceiving the patient or of putting off important treatment for fear of alarming the patient. There are doctors who regularly tell their patients that their blood pressure is lower than it actually is. A little thought would show these physicians that their patients will see other doctors and that all doctors cannot hope to dissemble equally. It is far better to teach the patient that daily or hourly fluctuations in blood pressure may be so great that there is little significance in any single reading [6] and that therefore he is better off not knowing what it is.

LITERATURE

Internists will be interested in reading some of the excellent recent books on psychotherapy, such as the works of Levine,[7] Strecker and Ebaugh [8] and Oscar Diethelm.[9] He should be familiar with the Minnesota experiment described by Smith.[10] An extremely inter-

4. Wolf, S., and Wolff, H. G.: Evidence on Genesis of Peptic Ulcer in Man, J. A. M. A. **120**: 670 (Oct. 31) 1942.
5. Means, J. H.: Thyroid and Its Diseases, Philadelphia, J. B. Lippincott Company, 1937.
6. Thomas, H. M., Jr.: Management of Early (Beginning) Essential Hypertension, M. Clin. North America **23**: 487 (March) 1939.
7. Levine, M.: Psychotherapy in Medical Practice, New York, The Macmillan Company, 1942.
8. Strecker, E. A., and Ebaugh, F. G.: Practical Clinical Psychiatry, New York, The Blakiston Company, 1940.
9. Diethelm, O.: Treatment in Psychiatry, New York, The Macmillan Company, 1936.
10. Smith, G.: Psychotherapy in General Medicine, New York, The Commonwealth Fund, 1946.

esting collection of contributions by forty psychiatrists, psychologists and internists interested in psychosomatic medicine is to be found in the two volume work edited by Hunt.[11] Dunbar's book[12] summarizes the field of psychosomatic medicine. Internists should not avoid some of the books written primarily for pediatricians, since the end results of behavior problems in childhood often are encountered in adult patients. One such book was written by Isaacs,[13] and a book that no one should miss is one by Kanner.[8]

The step from avoiding harmful malapropisms or destructive suggestions to making actual psychotherapeutic contributions and using suggestion constructively is not difficult. The psychologic aspects of every case should not be abandoned to psychiatrists, since internists are in better position to provide authoritative reassurance concerning the whole disease picture. Search for organic lesions must not be discontinued when psychotherapy is brought into the picture, because we all have seen cases in which neurotic symptoms have obscured serious organic disease.

HELPFUL TECHNICS

A simple method most medical practitioners find themselves using is a combination of suggestion and reasoning which is reinforced by their prestige and positive assertion. If the patient is to be helped he must be convinced by adequate explanation of the anatomic, physiologic and mental aspects of his case even though the explanation is tedious, time consuming and, often, difficult. It is improper to threaten the patient with dire results unless he obeys instructions, since this method is motivated by fear rather than reassurance.

Reassurance must be based on truth, since a structure built of falsehoods breaks down soon or late. Cabot[14] felt very strongly on this point. However, we must constantly remind ourselves that what appears to be the truth of medical explanation today may be far from the truth tomorrow. Also, the words we utter as a true statement may be interpreted by the patient to mean something entirely different. There can be no sure way of reaching or imparting a durable absolute truth. Therefore, we should be careful not to force on an unwilling patient disagreeable or alarming statements which we think are true. Gentle probing into the patient's attitude and wishes will reveal the correct course to pursue in his particular case and how much definite information he needs and really desires. Hope need never be completely destroyed even though false hope should be removed lest patients with irreversible lesions continue a futile quest for unattainable cure.

It is impossible to overemphasize the value of hope to the patient. Hopefulness developed through a true understanding of the symptoms can be translated into a desire for and an effort toward improvement.[15] Solomon knew the importance of this when he said in the Book of Proverbs, "Hope deferred maketh the heart sick: but when the desire cometh, it is a tree of life."

An ill timed effort at humor may infuriate or wound the patient, yet the physician's sense of humor is a magnificent therapeutic instrument. Unfortunately, psychiatric instruction gives us little or no help in its use. If the doctor can find a neutral object about which he and the patient can laugh, then the tension is lessened and a sense of friendliness and common purpose established. The introduction of humor must not conflict with the serious and thorough consideration of the patient's complaints. We may not be too casual on the one hand or too much concerned on the other. The only sure way of reaching the proper attitude is to understand the patient's thoughts and anxiety reactions and to watch very closely the nature of his responses with a sensitive appreciation of what persons usually worry about in the particular situation.

11. Hunt, J. M.: Personality and Behavior Disorders, New York, The Ronald Press Co., 1944.
12. Dunbar, H. F.: Emotions and Bodily Changes, ed. 3, New York, Columbia University Press, 1946.
13. Isaacs, S.: The Nursery Years, New York, The Vanguard Press, Inc., 1938.
14. Cabot, R. C.: Use of Truth and Falsehood in Medicine: Cartright Lectures, New York Academy of Medicine, December 1902.
15. Menninger, K., and Menninger, J. L.: Recreation for Morale, Bull. Menninger Clin. 6: 96 (May) 1942.

SUMMARY

Psychotherapy is treatment of the patient through his mind. I have not attempted to describe current technics used by psychiatrists. My purpose has been to justify psychotherapy as an integral part of every contact with patients and to indicate each physician's obligation to participate. This can be accomplished efficaciously only by keen awareness of accepted psychosomatic and psychiatric concepts and by a well integrated approach to the human being who is ill.

ABSTRACT OF DISCUSSION

DR. FRANCIS J. GERTY, Chicago: Dr. Thomas is to be congratulated on his valiant effort to attempt to tell you what psychotherapy is. A great many things have been called psychotherapy, and a great many things that have been psychotherapy have been called something else. Many years ago when I was a resident, an eminent neuropsychiatrist used to call on me to take his practice when he went on vacation. This man was successful in treating patients with functional disorders. He did not believe much in psychotherapy, beyond the fact that the physician should be a man of character and be honest with his patient. He did believe that psychoneurotic patients needed a sedative, a tonic and an increase in the supply of iodine sometimes, so he had a certain sedative mixture to which the druggist appended his name. He gave them sodium cacodylate by mouth. When he died, people in his office used to send his patients to me; I lost all of them, because his remedies did not work with me. The patients came to the conclusion that this man had had some secret formula and that that had died with him. The secret ingredient was the man, and this is an ingredient in all psychotherapy. We can apply the term "psychotherapy" to a great many things—placebo, bedside manner, reassurance, suggestion, hypnosis and psychoanalysis—but all of this is not very helpful when we attempt to make psychotherapy useful in our practice. We must look on psychotherapy, or at least psychotherapists, much as we look on the other remedies, as far as testing them out and weighing them are concerned. We are just beginning to look at psychotherapy this way. We are trying to examine honestly what elements enter into the matter of psychotherapy. There is an unconscious factor in psychotherapy which must be studied and of which we must become much more conscious. It is more important that the physician remove these in himself than that he set about removing them in the patient. This means that he must have a definite feeling for his patient; the patient will reciprocate with feeling on his part, and with this mutual feeling psychotherapy can be carried forward intelligently.

DR. THOMAS: I believe that the two points that have impressed me most in considering this general subject are: First, the psychologic aspects of treatment of the patient should always be present in the physician's mind, and, second, we must not allow our approach to the patient's psyche to remain amateurish, but by reading and thinking about it we must develop a superior type of psychotherapy which has its foundations on sound internal medicine.

EVALUATION OF CANCER CONTROL METHODS IN CONNECTICUT

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Analysis of the first total tables from the record registry in Connecticut enables one to evaluate cancer control methods for the past twelve years. The sources of factual information are the death rates, the attendance of patients with cancer at the clinics or general hospitals, the intervals of delay between symptoms and treatment and the attendance of physicians in the mutual educational program.

The age-adjusted cancer death rates are shown in table 1.[1]

The age-adjusted male cancer death rate has risen during the twelve year period, but appears to be leveling. The female age-adjusted cancer death rate has fallen. Since the average duration of life of all cancer patients is two years from the onset of the disease, the mortality rates of any year actually are a measure of events of two years before a retroactive index of progress. With this thought in mind, the gradual leveling of the total age-adjusted mortality rates in Connecticut is an encouraging sign.

The incidence rate of cancer as recorded in the record registry has increased with consistency, as shown in table 2.

The increase in the incidence rates as demonstrated in this table reflects the improvement in services rendered to persons in this state by every new measure introduced to increase the understanding of cancer. Within two years of the establishment of the division for cancer in the State Department of Health, a remarkable increase in hospital and clinic attendance of persons with cancer was noted. The publicity attendant on and the effort made by this new unit was undoubtedly responsible for this. In 1938, with the active organization of the Association of Connecticut Tumor Clinics and the attendant establishment of new clinics, another big increase in recognized treated cancer occurred. In 1941, the distribution of state funds to each of the general hospitals, the systematic backtracking of all cancer from 1935, the development of the state record registry and the establishment of universal follow-up of all cancer patients through the Division of Cancer and Other Chronic Diseases resulted in a dramatic increase in recognized treated cancer. In 1944, with the first successful drive of the Connecticut Cancer Society on a statewide basis, another increase occurred in recorded new cases of cancer. In 1946, with the inauguration by the Division of Cancer and Other Chronic Diseases of the popular and instructive Mutual Education Program, whereby four times a year three physicians from each general hospital visit another general hospital in the state and attend its cancer clinic, another increase in recognized cancer occurred. It was felt from an evaluation of the results on the records in the record registry that the general level of medical service was high in this state and that, by sharing, the whole level could be raised more quickly than by any other method. The token remuneration and expenses paid to each visiting physicians are furnished through the State Department of Health. All of these improvements have been made by the consistent effort to expand existing facilities to adequacy in the most universal and least disruptive way and with as little additional expense as possible.

The total incidence rates suggest but do **not** give sufficient detail to make clear the extent to which this voluntary registry of cancer has become adequate for obtaining the true picture of cancer morbidity. Checks with the death records and contacts with surrounding states and famous medical clinics make it possible for nearly every case of cancer to be known to this registry. Hospital insurance held by an estimated 40 per cent of the population of the state has encouraged the ready use of these facilities even by some persons who might not actually need hospital care. It is realized that cases of cancer of the skin treated in physician's offices are missed. Despite this, 9.5 per cent of cancer reported to this registry is cancer of the skin. Table 3 gives the incidence rates per 100,000 population in Connecticut by site and sex for the year 1945. This gives a clear picture of the size of the problem as it pertains to new cases.

TABLE 1.—*Age and Sex Adjusted Mortality Rate*
Connecticut 1935-1946, per 100,000

Year	Mortality Rate		
	Male Patients	Female Patients	Total
1935	102.9	120.3	111.6
1936	103.7	115.3	109.3
1937	101.2	114.0	107.3
1938	113.7	117.1	114.9
1939	108.6	116.8	112.3
1940	117.9	119.7	118.3
1941	115.6	120.2	117.6
1942	116.4	121.0	118.0
1943	113.8	121.9	118.4
1944	111.5	124.5	118.5
1945	120.7	119.2	118.9
1946	118.6	119.6	119.1

TABLE 2.—*Incidence Rates for Cancer*
Connecticut 1935-1946, per 100,000

Year	Incidence Rates	
	Male Patients	Female Patients
1935	114.5	145.9
1936	123.8	145.8
1937	127.4	166.3
1938	142.1	172.2
1939	162.4	198.1
1940	167.3	183.9
1941	179.8	207.2
1942	190.9	215.8
1943	194.9	229.1
1944	217.0	251.1
1945	229.4	259.5
1946	254.2	260.6

A follow-up over a long period of time is a requirement if accurate appraisal is to be attempted in studying cancer control methods, since the end results of cancer cannot be obtained until years after the onset of the original lesion. The staff of the Division of Cancer and other Chronic Diseases has trained new workers and guided experienced ones in hospital after hospital in the technics of obtaining follow-up.[2] Since over half of all cases recorded in the registry are private cases, ingenious and tactful procedures had to be evolved to reach this frequently unfollowed group. It was found when the system of follow-up was finally general that over 1,500 patients treated for cancer from 1935 through 1940 had had no follow-up from the time of the discharge after initial treatment. Since that time, the proportion of untraced cases has been so small that

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Aided by a grant from the United States Public Health Service of the Federal Security Agency.

1. Macdonald, E. J.: The Meaning of Adjusted Rates for Cancer, Connecticut Health Bull. **60**: 279 (Dec.) 1946.

2. Griswold, M. H., and Macdonald, E. J.: Cancer Record Registry—How It Functions, Connecticut M. J. **11**: 344 (May) 1947.

there are fewer than 5 per cent of the nearly 38,000 cases in the registry lost to follow-up.

From January 1935 through December 1946, in this state of less than 2,000,000 population, there have been 37,863 persons with cancer treated and diagnosed for the first time, for whom there are records in the local hospital cancer record registry and in the state total cancer record registry. There are more females than males in Connecticut, especially in the older age groups. There are, therefore, more cases of some sites of cancer among females than would occur if the sex ratio were even. The Connecticut registry uses as an origin the appearance at the hospital or clinic because normally, if a diagnosis of cancer is made or suspected, the patient is admitted for treatment either simultaneously or within a few days.

The percentage of male and female patients treated within one month, four months and six months of first symptoms is shown in table 4.

About one fifth of both male and female patients over the entire period have been treated within one month of first symptoms. About 40 per cent of both groups are treated within four months of first symptoms, and about half are treated within six months of first symptoms.

The survival rates are the criteria of measurement used [3] in discussions of the over-all cancer picture in this registry. For each of the sites as it is studied separately, a clinical check within weeks of presentation of the study will be sought of all patients living, to determine with reasonable accuracy the rate of cure as well as the survival rate. A patient not checked clinically within twelve months of any report of this registry is considered untraced. In order for a patient to be declared cured, however, an immediate check of each case is a necessity; so many factors alter the accurate description of cures and survivals. The age of the patient is so high at the time of onset and treatment that frequently death from other causes precludes determination of the results of cancer therapy. The average age at the time of treatment in Connecticut for the total period for female patients is 55.4 years and for male patients 59.6 years. Buried in this average is a wide and surprising range of years at the time of treatment according to the site of cancer and sex. Table 5 gives the average age at the time of treatment by selected sites of cancer.

TABLE 3.—*Incidence Rates for Cancer by Site by Sex* *

1945, per 100,000

Site	Incidence Rates		
	Male	Female	Total
Skin			
Skin of head and neck	22.0	15.8	18.9
Skin of upper extremities	2.9	0.9	1.9
Skin of trunk	3.8	2.0	2.9
Skin of lower extremities	0.9	0.9	0.9
Skin (generalized, multiple or location not specified)	1.1	0.3	0.7
Total	30.8	19.9	25.4
Soft parts			
Soft parts of head and neck	0.8	0.5	0.6
Soft parts of upper extremities	0.6	0.3	0.5
Soft parts of trunk	0.9	0.5	0.7
Soft parts of lower extremities	0.7	0.6	0.6
Soft parts (generalized, multiple or location not specified)	...	...	...
Total	2.9	1.8	2.4
Skeletal system			
Skull (including tumors of dental origin)	0.3	0.8	0.6
Spine (excluding sacrum and coccyx)	0.2	0.1	0.1
Bones of upper extremities, scapulas and clavicles	0.5	0.5	0.5
Bones of thorax (ribs, sternum)	...	0.1	0.00
Pelvis (including sacrum and coccyx)	...	0.3	0.2
Bones of lower extremities	0.2	0.6	0.4
Bones of skeleton (generalized, multiple or location not specified)	0.8	0.5	0.6
Joints and synovial membranes	...	0.1	0.1
Total	2.0	2.9	2.5
Central nervous system			
Brain and membranes	3.9	3.4	3.6
Spinal cord and membranes	0.6	0.3	0.5
Total	4.6	3.7	4.1
Upper respiratory and alimentary tracts			
Lip	5.5	0.9	3.2
Mucosa of cheek	0.8	0.2	0.5
Gingiva (or gum)	0.2	0.2	0.2
Palate	0.6	0.1	0.3
Floor of mouth	0.9	...	0.5
Tongue	2.3	0.7	1.5
Tonsil	0.6	0.3	0.5
Nasal cavity	0.2	0.2	0.2
Nasopharynx	0.6	0.1	0.3
Pharyngeal wall	0.7	0.3	0.5
Extrinsic larynx	3.1	0.5	1.8
Intrinsic larynx	1.6	0.3	0.9
Paranasal sinuses	1.0	0.3	0.7
Oral mucous membranes or mouth cavity (generalized, multiple or location not specified)	1.6	0.6	1.1
Total	19.7	4.9	12.3
Miscellaneous structures of head and neck			
Eye, orbital cavity and conjunctivas	0.6	0.8	0.7
Mastoid cells and middle and inner ear	0.1	0.2	0.2
Salivary glands	2.5	2.8	2.6
Thyroid and parathyroid	0.2	2.4	1.3
Total	3.4	6.2	4.8
Breast			
Breast	1.4	67.5	34.5
Nipple	...	0.1	0.06
Total	1.4	67.6	34.5
Viscera of the chest cavity			
Trachea, bronchial tree and lungs	19.0	2.6	10.8
Heart, pericardium and aorta	...	...	...
Esophagus	6.8	1.7	4.3
Mediastinum	0.6	0.8	0.7
Total	26.4	5.1	15.7
Abdominal cavity viscera			
Diaphragm, peritoneum, mesentery and unclassified abdominal tumors	1.3	2.3	1.8
Stomach	22.2	10.9	16.5
Liver, gallbladder and ducts	2.5	3.2	2.8
Pancreas	6.3	5.3	5.8
Spleen	...	0.1	0.06
Small intestine	1.0	1.4	1.2
Large intestine, right	5.7	8.2	6.9
Large intestine, left	14.7	12.4	13.4
Large intestine (generalized, multiple or location not specified)	3.4	4.9	4.1
Rectum	10.9	9.3	13.1
Anus	0.2	0.2	0.2
Total	74.2	61.9	68.0
Urinary tracts,			
Kidney	3.6	3.3	3.5
Adrenal	0.2	0.1	0.2
Ureter	...	...	...
Urinary bladder	10.4	4.3	7.4
Urethra	0.3	0.5	0.4
Total	14.7	8.2	11.4
Genital tract and external genitalia, male			
Prostate, seminal vesicles and adnexa	23.4	...	11.7
Glans and foreskin of penis	0.3	...	0.2
Testis, epididymis, spermatic cord	1.4	...	0.7
Total	25.1	...	12.6
Genital tract and external genitalia, female			
Corpus of uterus	...	20.0	10.0
Cervix of uterus	...	27.9	13.9
Ovaries	...	9.9	4.9
Fallopian tubes	...	...	...
Vagina	...	0.6	0.3
Labia minora and clitoris	...	0.7	0.3
Total	...	59.2	29.6
Systemic diseases			
Total	13.9	9.1	11.5
Metastatic cancer (generalized), no primary site discovered	10.1	8.9	9.5
Grand total	279.4	259.5	244.5

* The nomenclature used is the nomenclature of diagnoses of the Memorial Hospital for the treatment of cancer and allied diseases, New York.

3. Macdonald, E. J.: Survival Rates of Individuals Who Have Had Proved Cancer in Connecticut—1935-1942, Connecticut Health Bull. 58:2 (Nov.) 1944.

The proportionate age distribution by sex for total cancer is given in table 6. Comparable proportions are given by sex for those persons living as of April 1947. Among male patients 29.6 per cent of the total were between 60 and 69 years of age at the time of treatment,

TABLE 4.—*Percentage of Cancer Patients Receiving Treatment Within One, Four and Six Months of First Symptoms*

	Percentage of Patients					
	One Month		Four Months		Six Months	
Year	Male	Female	Male	Female	Male	Female
1935	19.1	18.4	38.1	39.5	47.0	50.3
1936	19.7	20.3	37.5	37.0	47.8	49.7
1937	1[illegible].6	20.9	37.6	40.4	47.2	5[illegible].1
1938	19.7	22.4	38.2	40.0	50.9	4[illegible].6
1939	21.7	20.6	39.9	39.7	49.3	49.2
1940	23.9	20.4	41.0	40.2	50.6	51.4
1941	24.3	25.3	41.0	43.2	50.6	51.2
1942	25.3	25.3	42.6	44.3	5[illegible].7	5[illegible].2
1943	25.0	24.7	41.6	43.2	51.7	53.0
1944	23.3	22.4	42.7	43.5	52.1	52.0
1945	24.1	20.1	42.1	40.6	51.6	50.5
1946	23.8	20.6	42.8	40.2	50.9	48.8

TABLE 5.—*Average Age at Time of Treatment by Selected Sites of Cancer*

	Average Age of Patients	
	Male	Female
Skin of head and neck	64.6	62.7
Skin of upper extremities	64.9	57.9
Skin of trunk	59.7	59.3
Skin of lower extremities	57.3	46.4
Skin (generalized)	62.8	51.0
Lip	6[illegible].1	6[illegible].4
Tongue	61.3	57.5
Intrinsic larynx	62.0	57.5
Eye	49.6	57.4
Breast	58.1	55.8
Lungs	57.2	58.3
Large intestine (right)	57.7	55.8
Large intestine (left)	60.9	58.9
Large intestine (location not specified)	59.6	58.9
Rectum	56.5	57.7
Kidney	54.5	50.8
Urinary bladder	62.6	64.4
Prostate	70.4	....
Testis	38.5	....
Corpus of uterus	....	57.3
Cervix of uterus	....	51.5
Ovaries	....	52.1
Total	59.6	55.4

19.9 per cent were between 70 and 79 and 4.7 per cent were over 80. Among female patients, 23.8 per cent were 60 to 69 years of age, 12.6 per cent were from 70 to 79 and 2.7 per cent were over 80 at the time of treatment. The survival rates among male patients are lower than among female patients. When it is observed that one fourth of all male patients in the registry came for treatment or diagnosis after the age of 70, one extremely important probable cause for a shorter period of survival becomes apparent. Another 29.6 per cent were between 60 and 69 at the time of treatment or diagnosis.

Comparison of the totals of the average age at the time of treatment and the percentage distribution of male and female patients living as of April 1947 shows the living as slightly younger, but without as great a difference as was expected.

One of the most encouraging features of a functioning registry which includes active follow-up of all living patients is the knowledge of the large number of persons who have survived treatment for cancer for more than five years. In Connecticut, there are over 3,000 living five to twelve years after treatment. Expressed another way, there are 174.5 persons out of every 100,000 in the population who have survived treatment for cancer for more than five years—128.9 per 100,000 males and 220.1 per 100,000 females. Also living in Connecticut are 9,000 other persons who have been treated for cancer within the last five years. Each passing year a larger number and a larger percentage of the total reach the five year survival mark, which often means safety.

Over the twelve year period under study, the total cancers have been grouped by site and by sex to determine the percentages of cancer of accessible sites in their relative proportion to the whole series. Table 7 gives the percentage distribution by sex and by site of certain cancers normally considered accessible.

One third of the cancers among male and two thirds among female patients are accessible. To the improvement of the prognosis of these types of cancer every educational effort should be bent. A recent study [4] measuring changing reasons for delay by certain sites of cancer between 1938 and 1946 shows that this effort is being made and is making measurable progress.

It is apparent that the greatest increase in those that come for treatment as soon as they notice symptoms has been among persons with cancer of the respiratory tract, the skin, rectum, buccal cavity and stomach, in that order.

The greatest improvement in the adequacy of medical advice has been among patients with cancers of the breast, stomach, other digestive organs and genitourinary system. The reduction in delay due to negligence and ignorance has been most pronounced in persons with cancers of the rectum, genitourinary system, other digestive organs (table 8, item 5) and respiratory tract, in that order. An increase in 1946 is noted, however, in delay due to negligence on the part of patients with cancer of the skin.

TABLE 6.—*Percentage Distribution of Cancer by Age and Sex*

1935-1946

Age Groups	Total Male Patients	Male Patients Living as of 1947	Total Female Patients	Female Patients Living as of 1947
0-9	1.3	1.1	0.7	0.4
10-19	1.1	1.3	1.1	1.1
20-29	2.6	2.7	2.8	3.5
30-39	4.4	5.4	8.7	9.6
40-49	10.7	11.5	20.5	22.5
50-59	24.4	24.3	25.9	25.2
60-69	29.6	30.0	23.8	22.9
70-79	19.9	21.7	12.6	13.0
80+	4.7	....	2.7	....
Unknown	1.3	2.0	1.2	1.8
Total	100.0	100.0	100.0	100.0
Average age (yr.)	59.6	58.3	55.4	55.3

TABLE 7.—*Percentage Distribution by Sex and by Site of Certain Cancers Normally Considered Accessible*

1935-1946

Sites	Percentage of Cancers	
	In Male Patients	In Female Patients
Skin	12.0	7.3
Upper respiratory and alimentary tract	10.8	1.6
Eye, thyroid, etc.	1.4	1.8
Breast	0.4	25.3
Rectum	6.5	3.9
Anus	0.07	0.07
Corpus	....	7.7
Cervix	....	11.1
Ovaries	....	5.7
Other parts of female genital tract	....	0.67
Total	31.17	65.14

4. Macdonald, E. J.: Changing Reasons for Cancer Patient Delay, Connecticut Health Bull. 61:99 (April) 1947.

Table 9 lists the proportion of cancers in the registry in the digestive tract and in the viscera of the chest cavity, generally less favorable in end result because early diagnosis is so difficult and adequate treatment depends on early diagnosis.

TABLE 8.—*Reasons for Delay by Site of Cancer*

Site	No Delay		Inadequate Medical Advice		Negligence and Ignorance		Total No. of Cancers in Series	
	1938	1946	1938	1946	1938	1946	1938	1946
All sites	10.6	38.2	12.1	2.9	33.8	26.5	1,000	1,000
Breast	16.1	45.6	15.0	3.3	38.9	32.2	180	180
Stomach	7.4	30.5	9.5	3.2	24.2	21.1	95	95
Rectum	6.1	34.8	15.2	6.1	37.9	19.7	66	66
Other digestive organs	16.7	45.2	9.5	1.2	28.0	19.6	168	168
Respiratory system	1.7	46.7	20.7	5.2	22.4	13.8	58	58
Genitourinary system	11.1	36.2	12.6	2.5	36.7	23.6	199	199
Buccal cavity	6.5	36.1	8.7	2.2	43.5	43.5	46	46
Skin	2.1	20.2	5.5	2.1	59.4	51.2	94	94
All others	10.6	44.7	13.8	3.2	31.9	19.1	94	94

TABLE 9.—*Percentage Distribution of Cancer of Selected Sites*

1935-1946

Site	Percentage Distribution	
	Male	Female
Viscera of the chest cavity	9.1	1.9
Abdominal cavity viscera (excluding rectum and anus)	27.13	18.93
Total	36.23	20.83

There has been a decided increase in diagnosed cancer in both these groups since 1935. This has been more apparent since 1940. Among male patients, there has been an average of 18.7 cases of cancer of the thoracic cavity viscera for each of the seven years from 1940 through 1946. The actual incidence rate for 1945 was 26.4 per 100,000 males. The incidence rate for males for cancer of the abdominal cavity viscera, exclusive of the rectum and anus, averaged 51.0 per 100,000 for seven years and actually was 57.1 per 100,000 for 1945. Among females in the same group, the average incidence rate for seven years was 42.3 per 100,000 while the actual incidence rate for 1945 was 52.4 per 100,000.

The increase or decrease in the other sites of cancer is shown in table 10. The increase is pronounced in cancer of the skin among male patients. It is more gradual in cancer of the rectum and cancer of the male genital and urinary tracts. It is interesting to notice that the rates for cancer of the skeletal system, the upper respiratory tract, the anus and the central nervous system are stationary or beginning to decline. Among female patients, the same thing has happened in cancer of the soft parts, the central nervous system and the anus and metastatic cancer with no primary site discovered. This last observation is particularly encouraging and appears to be consistent year after year. The over-all incidence rates for cancer show an increase of 35.0 per 100,000 among males and 38.3 per 100,000 among females between the seven year average and the 1945 actual experience.

To know the size of the problem, to have an established follow-up system, to have available diagnostic and therapeutic resources, to have an alert medical profession and an aroused laity and to have a division of cancer control capable of tabulating and analyzing these factors are all prerequisites to the final evaluation, which is measured in lives saved, in improving the rate of survival. Table 11 shows the distribution of traced living patients, microscopically proved to have had cancer, alive at yearly intervals following treatment.

Improved preoperative and postoperative care, progressing medical skill in therapeutic technics, reduction in delay on the part of the patient and the physician and cooperation on an almost universal scale have implemented the formation of this record registry. In each year there is improvement in the percentage of survival. This may not be accounted for by the normal increase in the expectation of life of the over-all population, because the progressive increase in age at the time of treatment has been constant, thus absorbing this variable of over-all increased survival as has the five year average difference in age at the time of treatment for those that died within five years and those that survived. From 1935 through 1941, each of the years up to five years following treatment shows steady, and in some instances spectacular, improvement. In the years from 1941 through 1945, the improvement is so pronounced that the promise of an increased five or more year survival rate will be maintained.

TABLE 10.—*Incidence of Cancer by Selected Sites*

Rate per 100,000

Site	Incidence of Cancer			
	Male		Female	
	7 Year Average	1945	7 Year Average	1945
Skin	23.5	30.8	17.3	19.9
Soft parts	2.6	2.9	2.1	1.8
Skeletal system	2.1	2.0	1.8	2.9
Central nervous system	4.4	4.6	3.9	3.7
Upper respiratory and alimentary tracts	20.7	19.7	3.7	4.9
Miscellaneous structures of head and neck	2.8	3.4	4.2	6.2
Breast	0.7	1.4	62.6	67.6
Rectum	12.8	16.9	8.6	9.3
Anus	0.2	0.2	0.2	0.2
Urinary tracts	12.9	14.7	5.9	8.2
Male genital tract	22.6	25.1	...	...
Female genital tract	...	...	53.4	59.2
Systemic diseases	10.6	13.9	7.9	9.1
Metastatic cancer (no primary site discovered	8.8	10.1	9.9	8.9
Total	194.4	229.4	221.2	239.5

TABLE 11.—*Distribution of Traced Living Patients, Microscopically Proved to Have Had Cancer, Alive at Yearly Intervals Following Treatment*

By Cases and Percentages

Year of Admission	Total Treated	Alive Yr. of Treatment	Alive 1 Yr. Later	Alive 2 Yr. Later	Alive 3 Yr. Later	Alive 4 Yr. Later	Alive 5 Yr. Later
1935	1,399	912 65.2	593 42.4	472 33.7	397 28.4	345 24.7	309 22.1
1936	1,452	946 65.2	631 43.5	509 35.1	440 30.3	375 25.8	329 22.7
1937	1,622	1,098 67.7	729 44.9	552 34.0	453 27.9	406 25.0	361 22.3
1938	1,875	1,230 65.6	834 44.5	661 35.3	553 29.5	502 26.8	461 24.6
1939	2,096	1,424 67.9	967 46.1	780 37.2	683 32.6	608 29.0	565 27.0
1940	2,077	1,418 68.3	982 47.3	840 40.4	762 36.7	673 32.4	615 29.6
1941	2,465	1,745 70.8	1,280 52.0	1,089 44.2	906 39.2	879 35.7	825 33.5
1942	2,649	1,908 72.0	1,447 54.6	1,258 47.5	1,123 42.4	1,056 39.9	
1943	2,699	1,895 70.2	1,442 53.4	1,234 45.7	1,127 41.8		
1944	2,905	2,109 72.6	1,580 54.4	1,382 47.6			
1945	2,947	2,150 73.0	1,737 58.9				

Clinical Notes, Suggestions and New Instruments

ROCKY MOUNTAIN SPOTTED FEVER TREATED WITH AUREOMYCIN

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The occurrence of Rocky Mountain spotted fever due to infection with Rickettsia rickettsi in the eastern part of Long Island, N. Y., is not infrequent, because of the prevalence of the common vector Dermacentor variabilis, the dog tick. There are usually 10 to 15 cases each year in Suffolk County. The mortality of the disease is known to vary from year to year and in different parts of the country from 15 per cent to as high as 37.5 per cent in the Bitter Root Valley.

The following case is reported because of the striking and rapid result obtained with aureomycin, a new antibiotic which has been found to be extremely effective both in vitro and in vivo against rickettsial organisms of several varieties, as well as against certain viruses and bacteria. Aureomycin has been produced from a strain of Streptomyces aureofaciens isolated by Dr. B. M. Duggar of the Lederle Laboratories.

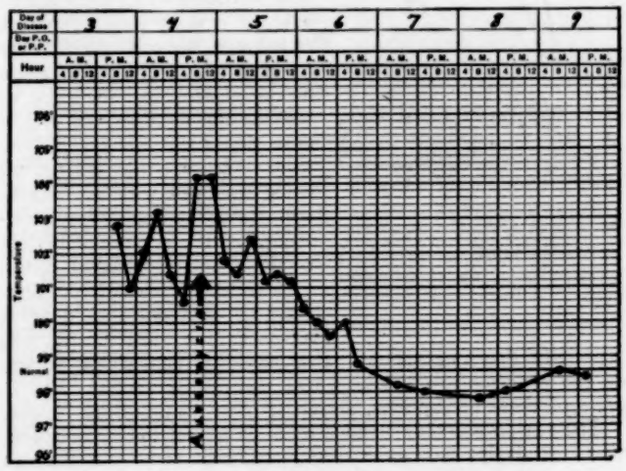
REPORT OF A CASE

A 28 year old white woman was admitted to the Huntington Hospital on July 19, 1948, with a three day history of severe headache, malaise and backache of rather sudden onset. There had been chills and temperature from 101 to 103 F., occasional nausea and vomiting and considerable photophobia. On the morning of admission she had noted a rash on her arms and legs. In the preceding two weeks she had found two or three embedded ticks on her body, the last about six days before onset of the illness. There had been no known exposure to possibly contaminated food or water, and there was no evidence of rat or louse infestation of her surroundings. The past history was entirely noncontributory.

Physical examination showed an acutely ill woman with a temperature of 103 F., pulse rate 120 and respirations 20. Diffusely distributed on the arms and legs there was a discrete pink macular rash, the lesions averaging 1 cm. in diameter. There were only a few on the trunk. The spleen was not palpable, and the results of the rest of the examination were entirely within normal limits. Initial laboratory work revealed a red blood cell count of 4,300,000, hemoglobin 12 Gm. and white blood cell count 8,500, with 75 neutrophils, 22 lymphocytes and 3 mononuclear cells. The urine was normal.

Rocky Mountain spotted fever was considered the most probable diagnosis, but, pending the result of blood culture to rule out meningococcemia, penicillin was given in doses of 300,000 units every six hours for three doses and then discontinued when the culture was reported to be negative. Through Dr. Yale Kneeland at Presbyterian Hospital, we were able to obtain a supply of aureomycin from Dr. Herald Cox of the Lederle Laboratories. Treatment with this was begun twenty-four hours after the patient's admission, on the fourth day of the illness, at which time the rash was more pronounced and violaceous and the temperature was spiking to 104 F. The dosage was 1 Gm. every six hours by mouth for forty-eight hours, at which time the temperature had returned to normal and the patient was dramatically relieved of all her symptoms. The aureomycin dosage was reduced to 0.5 Gm. every six hours for the ensuing twenty-four hours, making a total dose of 10 Gm. There were no symptoms or signs of toxicity, with the possible exception of mild nausea and vomiting for a few hours on the second day of treatment, which was transitory and probably due to other factors since it disappeared in spite of continued use of the drug. The patient continued to improve and was ambulatory, with the rash gone by the ninth day of the illness, and she was discharged from the hospital on the tenth day.

During her course two blood cultures were negative; urine and stool cultures revealed no pathogens. The blood cell count remained normal throughout. The Wassermann reaction of the blood was negative; nonprotein nitrogen was 39 mg. per hundred cubic centimeters, total protein 7.7, albumin 3.4 and globulin 4.3 mg. Serologic studies on the fourth day of the disease showed a negative Widal reaction, negative reaction to the complement fixation test for Rocky Mountain spotted fever and rickettsialpox, agglutination of Proteus OX19 to 1:40 and negative results with OX2 and OXK. On the tenth day, however, the reaction to the complement fixation test was positive for Rocky Mountain spotted fever in a titer of 88. This was confirmed by Dr. Cox at the Lederle Laboratories, who reported a positive result for Rocky Mountain spotted fever in serum dilution up to 1:64. The reaction to the rickettsialpox complement fixation test, which has been found to be somewhat more sensitive in detection of spotted fever early in the disease, also became positive by the tenth day, though in somewhat lower titer.



Temperature chart from the case reported.

COMMENT

It is felt that the prompt response to aureomycin therapy in this confirmed case of spotted fever, in which one would expect a severe febrile course of two to three weeks, is further evidence of the efficacy of this agent against the Rickettsia of Rocky Mountain spotted fever.

22 Oakwood Avenue.

From the North Shore Medical Group and Huntington Hospital.

A SAFE DIAGNOSTIC OPTICAL ESOPHAGOSCOPE

RUDOLF SCHINDLER, M.D.
Los Angeles

For a long time internists and surgeons have desired to possess an instrument with which the esophagus might be inspected safely and clearly. Esophagitis, a frequent cause of distress (Winkelstein), can be diagnosed only by direct inspection of the inflamed mucosa. Early carcinoma of the esophagus easily escapes roentgenologic detection.

DISADVANTAGES OF ESOPHAGOSCOPES NOW IN USE

The present esophagoscopes are not safe. Mastery of their use requires long study, but even in the hands of the most expert examiner occasional mishaps occur. The most frequent lesion is a hypopharyngeal tear, often leading to mediastinitis and death. Usually it is assumed that esophagoscopy has a morbidity rate of 2 per cent and a mortality rate of 0.5 per cent. These figures would rise considerably if esophagoscopy were to be done by any other than trained experts. The existing dangers attending esophagoscopic examination often prevent the most conscientious physicians from referring their patients for esophagoscopic study. Many esophagoscopists have also felt the need for diminishing the danger of esophagoscopic examination.

A tear of the hypopharynx is almost unknown following gastroscopy. Many thousands of gastroscopies have been done

Fellow of the American College of Physicians.
From the Department of Medicine, College of Medical Evangelists, Los Angeles.

by me and most other gastroscopists without any such untoward result. Only rarely is it reported as a curiosity. This is not only true of the present day flexible gastroscope, but it was true also in the days of the rigid gastroscopes. Hübner,[1] in a study on the dangers of gastroscopy in the time of the rigid gastroscope, stated that practically all accidents involved the thoracic esophagus, but no hypopharyngeal lesions occurred.

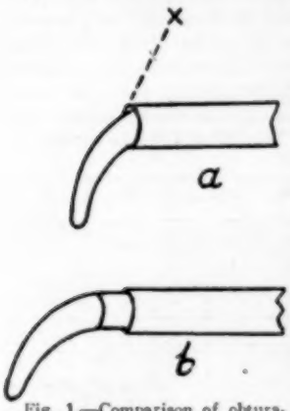


Fig. 1.—Comparison of obturator tips: *a*, faulty, and *b*, correct construction of tip of obturator, with *x* indicating the free dangerous edge.

This astonishing difference between esophagoscopy and gastroscopy is chiefly due to the different principle of introduction used in the two procedures. The introduction of the esophagoscope is done under guidance of the eye, the instrument being an open tube. The introduction of the gastroscope, the rigid as well as the flexible, was and is done under the guidance of the tactile sense, the instrument being equipped with an obturator. Esophagoscopists have contended that lesions could not occur if the esophageal lumen were constantly visualized. They warned[2] that one should never advance the instrument and especially that one should never pass the constrictor muscle of the pharynx if the lumen was not plainly visible. But in spite of these precautions, accidents have continued to happen.

The reason becomes obvious by a simple anatomic consideration. Nobody has ever suggested that one introduce a proctoscope as an open tube under visual guidance. If it were tried, lesions of the sphincteric portion of the rectum would occur, for it is closed by a strong sphincter muscle. It can be opened slightly if the patient is asked to press, but this opening usually is insufficient and may disappear at any moment. Disengagement of the walls of this canal by the use of an obturator is, however, simple.

The conditions at the entrance to the esophagus, though not identical, are similar. There, also, a powerful sphincter muscle is present. It is more frequently open than the anal sphincter muscle, yet it often is tightly closed. It may open after a swallowing movement, and therefore it has been recommended that the open esophagoscope be passed as the patient makes a swallowing movement. But this opening may be of very short duration only; it is easily missed, and it may be absent in apprehensive and spastic patients. Then a slight movement of the open instrument will produce the dreaded lesion.

An instrument bearing a soft rubber obturator may encounter three different situations: (1) The constrictor muscle of the pharynx may be open; then the instrument will enter the esophagus without resistance. (2) The muscle may be closed, but not spastically; then the rubber obturator will take over the function of the metal obturator of the proctoscope, it will gently and without danger disengage the walls and permit the metal tube to follow. (3) The muscle is spastically closed, in which circumstance no instrument can be introduced and its relaxation must be awaited. A rubber obturator, even under pressure, will bend but will not produce a tear. In the first and second instances an open tube is dangerous, a tube closed with a flexible obturator is safe, as ten thousands of examinations with the rigid gastroscope have proved.

It must be admitted that in times past mishaps occurred when esophagoscopes carrying an obturator were used. The reason for these mishaps is apparent. It was the size of these old tubes which was responsible for the accidents. At the entrance of the esophagus an anteroposterior diameter of about 15 mm. can rarely be exceeded. Instruments of times past had this maximum diameter. But in spastic and restless patients the very size of the instrument became dangerous. Esophagoscopists, therefore, reduced the size, and the present day standard Jackson esophagoscope has an outer diameter of only 10 to 13 mm. The rigid Schindler gastroscope of 1922 had a diameter of 11 mm., and no pharyngeal lesions were observed with this instrument.

These facts have been known to many observers. Henning[3] constructed a closed esophagoscope in 1932. Boros[4] in 1947 described an open esophagoscope the lower end of which is a flexible metal spiral. It is to be introduced blindly and probably often can be introduced easily, but if the visual introduction is abandoned the retention of an open tube appears illogical and unnecessary. In fact, each open esophagoscope can be changed into a safe instrument by inserting a tightly fitting rubber obturator.[5] A precaution must be used, however, in such a simple construction. If a rubber obturator bends, an empty space will form between the obturator and the free edge of the metal tube. This free edge then would be a source of danger again. This is avoided by attaching the rubber finger on a metal rod which is a few mm. longer than the esophagoscope (fig. 1).

Thus it is easy to solve the problem of a safe inspection of the esophagus, although such an instrument must not be used if lesions immediately below the constrictor muscle of the pharynx have been recognized at roentgen examination. There is the problem of the clear inspection left. As mentioned, for reasons of safety the diameter of the esophagoscope had to be much reduced. Consequently the picture seen at the end of the long tube is a small one. Its interpretation therefore can be difficult. Some mucus or blood may make the examination still more difficult. If there is a pathologic prominence, biopsy is usually required to determine its nature. This condition seems unsatisfactory to the internist who is used to the brilliant pictures of cystoscopy and gastroscopy.

A NEW ESOPHAGOSCOPE

The idea of constructing an esophagoscope having an optical system was conceived. It is not a new idea, however. It was, among others, tried by Glücksmann[6] and by Henning. Two solutions had to be considered, namely, to construct either an outer optical attachment or an optical system to be introduced into the esophagoscopic tube itself. The latter, more difficult way was chosen because of the more brilliant pictures and the better magnification available. The chief problem was to keep the esophageal mucosa away from the optical objective. This was solved by the construction of two metal shells covering the objective at introduction and being spread after introduction. Thereby the mucosa is removed to the proper distance. The objective itself had to be constructed different from that of a cystoscope or gastroscope. In the esophagus, side views could be of no avail. One has to look forward into a tube, and the prism used in cystoscopy and gastroscopy had to be

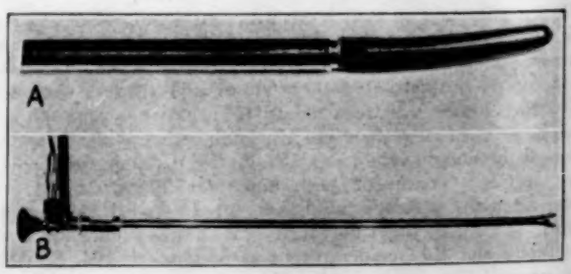


Fig. 2.—*A*, tip of instrument with obturator. *B*, instrument after removal of obturator and insertion of optical apparatus. Shells are spread to remove mucosa from objective.

abandoned in favor of a forward-looking objective lens. It seemed questionable whether it would be possible to keep such a lens clean, since one might think that it would be easily smeared by esophageal secretion. Preliminary attempts with a makeshift instrument in 1943 at Cook County Hospital, Chicago, proved that with the proper position of the patient

1. Hübner, A.: Gastroskopie, Jena, Gustav Fischer, 1928.
2. Jackson, C., and Jackson, C. L.: Bronchoscopy, Esophagoscopy and Gastroscopy, Philadelphia, W. B. Saunders Company, 1934.
3. Henning, N.: Ueber ein neues Oesophagaskop für den Gebrauch der inneren Klinik, Klin. Wchnschr. **11**: 1673, 1932.
4. Boros, E.: Flexible Tube Esophagoscopy, read before the American Gastroscopic Society, May 1948.
5. Howard, J. T.: Adventures in the Esophagus, South. M. J. **40**: 197, 1947.
6. Cited by Stark, H.: Lehrbuch der Ösophagoskopie, Würzburg, C. Kabitzsch, 1914.

and with the proper technic clear pictures could be obtained. Therefore such an instrument—a safe diagnostic optical esophagoscope—was constructed (American Cystoscope Makers, Inc., New York). It yields sharp pictures with high magnification, with which every detail can be readily recognized. This instrument is so thin (10 mm.) that the discomfort for the patient is minimal, if proper anesthesia is used (fig. 2).

Although the pictures seen are distinct and clear, it seemed desirable to add a biopsy forceps for the diagnosis in those cases in which an obstruction exists, but inspection does not permit the decision whether it is benign or malignant. This biopsy forceps is constructed also in junction with a magnifying optical system.

Similar optical attachments for an injection needle (treatment of varices) and a grasping forceps (extraction of foreign bodies) may be feasible and may change the diagnostic instrument into a therapeutic one.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following reports. HOWARD A. CARTER, *Secretary.*

OTARION HEARING AID MODEL E-2 ACCEPTABLE

Manufacturer: Otarion Hearing Aids, 159 North Dearborn Street, Chicago 1.

This instrument is a three tube air conduction hearing aid, with the batteries contained in the amplifier case. The case is constructed of die-cast magnesium alloy, coated with vinyl resin finish, ivory in color. A side-hinged full length back cover gives access to the battery compartments and the three tubes, which are readily accessible. The magnetic type receiver is connected to the amplifier case by means of a light plastic-covered cord which has dual pin plugs at each end.

Otarion Hearing Aid, Model E-2

Two wheel-type controls are placed at the top of the case. One is a volume control; the other is a combination "on-off" switch and tone control with three settings: 1 dot, full tone range; 2 dots, slight low frequency attenuation; 3 dots, greater low frequency attenuation. A detachable wearing or attachment clip fastens either to the front or the back of the case.

The Otarion Model E-2 contains a built-in voltmeter, called a Metrodyne, by means of which the voltages of either the A or the B battery can be checked whenever desired.

The dimensions are 133 by 64 by 33 mm. (5¼ by 2½ by ⅜ inches) and the weight is 170 Gm. (6 ounces). The A battery of the zinc and carbon type is 1.5 volts and the B battery of the zinc and carbon type is 30 volts. The A battery drain is 50 milliamperes and the B battery is 0.8 milliampere.

Acoustical Gain for Pure Tones (maximum gain in decibels for each of 6 frequencies and 3 settings of the tone control):

Position of Tone Control	Frequency					
	250	500	1,000	2,000	3,000	4,000 cycles
1 dot	51	55	62	63	65	50 db.
2 dots	46	53	61	63	65	50 db.
3 dots	40	48	58	63	65	50 db.

Acoustical Gain for Speech.—The maximum gain, when the tone control was set at the 1-dot position, was 55 decibels. This value was obtained on two different hard of hearing persons, each of whom is an experienced user of hearing aids and has approximately 60 decibels unaided loss for speech with a speech audiometer. These persons perceived speech with 55 decibels less intensity through a high quality sound amplification system (speech audiometer) in a sound-proof room with the hearing aid than without it. NOTE: This high gain for speech was obtained on experienced users of hearing aids with predominantly middle ear types of hearing impairments, which type of impairment obtains best results with hearing aids. This amount of gain with a hearing aid cannot be anticipated by persons with inner ear impairments.

The Council on Physical Medicine voted to include the Otarion Hearing Aid Model E-2 in its list of accepted devices.

POCKET SIZE ELECTRONIC STETHOSCOPE ACCEPTABLE

Manufacturer: American Medical Instrument & Supply Corp., 5 North Wabash Avenue, Chicago 2.

The Pocket Size Electronic Stethoscope is an instrument designed to amplify the sounds picked up during auscultation. It is roughly cylindric in shape and weighs about 225 Gm. (8 oz. avoirdupois). The length is 14 cm. (5½ inches), the diameter 5 cm. (2 inches) and the shipping weight 450 Gm. (1 pound). This does not include the necessary binaural fittings and rubber tubing. The needed electrical power must be supplied by a mercury type A battery and a 22½ volt zinc-carbon B battery.

Pocket size Electronic Stethoscope

The Council obtained evidence that the instrument had given satisfactory service in the hands of practicing physicians with normal hearing and that it gave increased accuracy of diagnosis in some cases. It was particularly helpful to physicians with impaired hearing.

The Council on Physical Medicine voted to include the Pocket Size Electronic Stethoscope in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORT TO THE COUNCIL

The Council has authorized publication of the following progress report from the Therapeutic Trials Committee.

AUSTIN SMITH, M.D., *Secretary.*

ACTIVITIES OF THE THERAPEUTIC TRIALS COMMITTEE

The Therapeutic Trials Committee was organized as a standing committee of the Council on Pharmacy and Chemistry and commenced its operations in April, 1946. Although considerable attention has been devoted to matters of organization and procedure during the intervening two and one-half years, a number of significant problems have been commenced under Committee auspices, and it is deemed appropriate to summarize briefly the accomplishments of the Committee and the investigators working under its aegis.

The work of the Committee can conveniently be divided into three sections: (1) investigations pursued under Committee contracts, (2) collaborative projects, and (3) educational and informational services. It must be emphasized that no problem undertaken by the Committee has as yet been completed and, therefore, detailed reports on Committee investigations cannot be presented. Comments on the general trend of these investigations are offered, but it should be understood that no conclusions are permissible until the research has been completed.

Investigations Pursued Under Committee Contracts

Because of the terms of the contracts, it is not possible to identify the investigators or the sponsoring firms involved in the investigations mentioned below. On completion of these investigations it is anticipated that full reports will be published by the authors for the benefit of the medical profession.

Streptomycin Therapy of Granuloma Inguinale.—Although several reports of the efficacy of streptomycin in the treatment of granuloma inguinale have appeared, it was felt desirable to encourage additional studies in order to determine, on a large number of patients, the precise usefulness of this agent. The

results so far reported to the Committee confirm the efficacy of streptomycin, but since the effective dose appears to be large, investigations are proceeding to determine whether combined streptomycin-antimony therapy may be more efficacious and less likely to induce undesirable side-actions.

Aludrine Sulfate (Isopropyl Epinephrine) Therapy of Bronchial Asthma.—Aludrine-Sulfate, a preparation first tried clinically in Germany during the last war, has been found to have a profound bronchodilator action in laboratory animals and, unlike epinephrine and ephedrine, to have a vasodilator action. It was thought desirable to investigate more thoroughly its effects in bronchial asthma.

Preliminary work indicates that it is not as potent in clinical asthma as is indicated by animal studies. Furthermore, when given by intramuscular injection or by mouth in doses sufficient to exert a significant bronchodilator effect, patients may experience typical anginal attacks and show electrocardiographic changes compatible with coronary constriction. There is some indication that these serious side-effects can be mitigated by administering the drug sublingually and by inhalation. A report has been submitted by the responsible investigators and will be published shortly.

Chlorophyll Therapy of Wounds and Ulcers.—Numerous reports have been published regarding the efficacy of solutions and ointments containing chlorophyll in decreasing the healing time of wounds and ulcers, particularly those which showed delayed healing or were indolent. In an attempt to secure a more critical evaluation of chlorophyll therapy, two investigations are being conducted under Committee auspices. The first, dealing with the actions of a solution and an ointment of chlorophyll on the rate of healing of wounds involves the use of a method originally devised by Smelo[1] and quantitative measurements of the rate are being made by a technic based on observations of Carrel and Hartman[2] and adapted by DuNouy.[3] In the small series of patients studied to date, 25 per cent have shown acceleration of wound healing. Where significant variables were eliminated, 37 per cent of the patients showed accelerated healing.

A second investigation involving the study of a chlorophyll solution in the treatment of certain chronic nasopharyngeal conditions is underway but no reports of progress have as yet been submitted to the Committee.

Methyl Cellulose as a Laxative.—Work is just commencing on a clinical study designed primarily to study various factors involved in chronic forms of constipation and to evaluate the possible usefulness of methyl cellulose as compared to other bulk-producing laxatives and lubricants.

Adjusted Ophthalmic Solutions.—Because of the unsatisfactory state of our knowledge concerning the optimum physical-chemical properties for solutions of drugs intended for ophthalmic use, a request was made to the Committee for an investigation of such factors as p_H, isotonicity, stability of the drug, etc., on the effect of these solutions on the human eye. Arrangements have been made for this investigation, and the work will get under way in the near future. The results of this study should be of importance not only to ophthalmologists but also to pharmacists and pharmaceutical manufacturers.

Collaborative Investigators

Two problems have been presented to the Committee which, because of their magnitude, have required the appointment of special subcommittees to plan and evaluate the investigations. Furthermore, the active collaboration of competent investigators has been necessary in order that all phases of these problems receive adequate exploration.

Estrogens and Androgens in Mammary Cancer.—A report outlining the background of this study has been published.[4] Forty-eight clinics are participating in this study. Each investigator is pursuing a problem of his own choosing, often in a larger field of research. In order to make his data available for pooling with those of others, he conforms to certain minimal requirements established by the Subcommittee on Steroids and Cancer, which permit him to choose one of several dosage schedules but require comparisons to be made with certain standard schedules. Certain minimal laboratory examinations are required on each patient, but the investigator is encouraged to use his own ingenuity and widen the problem in the direction wherein lie his own particular interests.

Four dosage schedules of testosterone propionate are being investigated in order to determine the minimum dose to produce definite effects on the primary tumor or its metastases. These are: 75 mg. weekly, 150 mg. weekly, 300 mg. weekly, and 600 mg. weekly. Testosterone therapy is being directed primarily against bony metastases although observation of the effects of this hormone on soft tissue lesions, especially in younger women, is being made.

Six different estrogens are also under study for their effects on soft tissue and bony lesions, particularly in older women. The estrogens and dosage being used are as follows: diethylstilbestrol, 15 mg. daily; dienestrol, 15 mg. daily; dimethyl ether of diethylstilbestrol, 30 mg. daily; ethinyl estradiol, 3 mg. daily; "premarin," 30 mg. daily; and estradiol dipropionate, 5 mg. three times in the first week and 5 mg. twice weekly thereafter.

A uniform system of reporting cases has been established and all case reports and progress reports will be reviewed and evaluated by the Subcommittee on Steroids and Cancer, composed of Dr. Ira T. Nathanson, Boston, Chairman, Dr. Frank Adair, New York, Dr. Willard Allen, St. Louis, and Dr. Earl Engle, New York. Through the courtesy of Col. J. E. Ash, the facilities of the American Registry of Pathology have been made available to the Committee and all pathologic material obtained at biopsy, operation, or autopsy of patients admitted to this study will be deposited at the Army Institute of Pathology as a permanent collection. This material will be reviewed and evaluated by three consultants in pathology: Dr. Howard T. Karsner, Cleveland, Dr. Fred Stewart, New York, and Dr. Shields Warren, Boston.

Similarly, duplicates of significant roentgenologic films will be prepared and deposited at the Registry of Roentgenologic Pathology, where they will be reviewed by three consultants in radiology: Dr. L. H. Garland, San Francisco, Dr. Leo Rigler, Minneapolis, and Dr. Merrill Sosman, Boston.

The active cooperation of the American Cancer Society through the Committee on Growth of the National Research Council and of The National Advisory Cancer Council of the United States Public Health Service has been secured. These agencies have reviewed applications for grants in aid from participating investigators and have in most instances granted the sums requested for carrying on this work. None of the funds so granted have been given to the Committee nor has the Committee sought financial assistance from outside sources to defray the expenses incident to the coordination of this project.

Fourteen pharmaceutical firms have agreed to supply large quantities of testosterone and estrogens to the Committee for use in this study. These firms have been most generous with these costly materials and their wholehearted cooperation is appreciated by the Committee. The cooperating firms are:

Abbott Laboratories.
Ayerst, McKenna & Harrison, Limited.
Ciba Pharmaceutical Products, Inc.
Charles E. Frosst & Co. (Canada).
Lakeside Laboratories, Inc.
Rare Chemicals, Inc.
Roche-Organon, Inc.
Schering Corporation
Schering Corporation Limited (Canada)
E. R. Squibb & Sons.
The Upjohn Company.
Wallace & Tiernan Products, Inc.
White Laboratories, Inc.
Winthrop-Stearns, Inc.

Although the actual investigations did not commence until March, 1948, more than 235 cases of breast cancer were under study by 26 investigators by the middle of October, as shown by case reports filed with the Committee. It is much too early to draw any conclusions regarding the palliative effects of these hormones in breast cancer. It can be said, however, that perhaps 20 to 25 per cent of the patients show some definite beneficial subjective or objective improvement. To be answered are such questions as the duration of palliation, particularly in comparison to the results known to occur following adequate roentgen irradiation; the physiologic or pathologic factors governing favorable responses; the mechanism by which regres-

1. Smelo, L. S.: Arch. Surg. **33**: 493, 1936.
2. Carrel, A., and Hartman, A.: J. Exper. Med. **24**: 429, 1916.
3. Du Nouy, P. L.: J. Exper. Med. **24**: 461, 1916.
4. Report of the Council on Pharmacy and Chemistry, J. A. M. A. **135**: 987, 1947.

sive changes in the tumors are brought about, and the most satisfactory preparations and doses to be used.

From time to time reports on this project will be published by the Committee and by the individual collaborators. The material from which these reports are prepared will be available to physicians and other scientists at the American Registry of Pathology in Washington, D. C.

Evaluation of Moist Heat in Poliomyelitis.—At the request of the National Foundation for Infantile Paralysis, the Committee agreed to investigate the feasibility of designing and conducting a coordinated clinical investigation to determine the precise value, immediate and remote, of moist heat in the treatment of acute poliomyelitis. A Subcommittee composed of Dr. William T. Green, Boston, Dr. Derek Denny-Brown, Boston, Dr. Hugo Muench, Boston, and Dr. James L. Wilson, Ann Arbor, was appointed. The Subcommittee drafted a preliminary report indicating that such a study would be feasible and outlined in general terms the experimental design for such a project. This report was submitted to The National Foundation, which subsequently requested the Committee to draft detailed plans and a budget for such an investigation for consideration by their Medical Advisory Committees.

The difficulties inherent in studying the effects of any therapeutic procedure in poliomyelitis are caused by the variability and unpredictability of the disease and by the emotional aura which surrounds the scientist seeking objective data in any condition which affects children or which produces crippling. These difficulties can be overcome only by the establishment of rigid controls in the clinical investigation and securing the cooperation of competent and critical investigators who will sacrifice their freedom of individual action in order to follow predetermined protocols established by the Committee.

Fortunately, several such investigators have been found who have indicated a willingness to participate in such a project if The National Foundation for Infantile Paralysis decides to proceed with the investigation outlined by the Committee.

Although all details of the investigative program have not been worked out, it is apparent that it will cost a great deal of money to do a properly critical investigation. One of the questions which The National Foundation will have to decide is whether the expected results of such a program will justify the expenditure of large sums of money.

Educational and Informational Projects

Besides the sponsorship of clinical investigations, the Committee is undertaking to collect information and publish reports of a general nature which may be of interest to the medical profession and to research workers. One such article, "The Cost of Clinical Research" has already been published.[5]

A group of Consultants in Statistical Methods has been formed, comprising Dr. J. Harold Austin, Philadelphia, Dr. Errett C. Albritton, Washington, Dr. George F. Badger, Cleveland, Dr. Ross L. Gauld, Washington, Dr. H. M. C. Luykx, New York, and Dr. Everett L. Welker, Chicago, who are considering the preparation of a series of articles on the design of experiments and the evaluation of data for the benefit of the medical profession.

More than forty institutions engaged in medical research have been visited by the Secretary of the Committee and the facilities and research interests of the investigators of these forty institutions have been tabulated and indexed.

Liaison has been maintained with the Food and Drug Administration, Research Grants Division of The National Institute of Health, and The National Research Council. An effective interchange of information of mutual interest has been established.

From time to time additional activities will be developed to make the Committee more useful to the medical scientist and to the profession in general. It is believed, however, that the activities of the Committee since its establishment two and a half years ago demonstrate the wisdom of the Council on Pharmacy and Chemistry in thus extending the scope of its interests.

CHESTER S. KEEFER, M.D., Chairman.
WALTON VAN WINKLE JR., M.D., Secretary.

5. Report of the Council on Pharmacy and Chemistry, J. A. M. A. **133**: 30, 1947.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

ROCKY MOUNTAIN SPOTTED FEVER VACCINE.—Vaccine prepared from membranes of embryonated chicken eggs infected with Rickettsia rickettsii. Rocky Mountain Spotted Fever Vaccine is prepared from a saline suspension of infected chick embryo membranes. The suspension, after inactivation with formaldehyde solution, is extracted with ether, according to a modification of the method of Craigie (*Canad. J. Res. E.*, **23**:104, 1945), to remove yolk lipids and tissue debris, yielding an almost water-clear solution which contains the immunizing antigen.

Actions and Uses.—There is considerable amount of evidence that a vaccine preparation is of value in the prevention of Rocky Mountain spotted fever (tick typhus), a rickettsial disease due to Rickettsia rickettsii which is widely ditsributed in the United States, being especially prevalent in Maryland, Virginia and North Carolina as well as in some parts of the Rocky Mountain regions. In the western United States the common vector is D. andersoni which is rarely found in urban centers; while in the eastern United States both urban and rural areas may be infested with the common vector, the dog tick, D. variabilis. The vaccine originally was made from artificially cultivated and infected ticks. More recently, this has been replaced by the infected membranes of the embryonated chicken eggs.

The vaccine leads to the development of active immunity, the duration of which is not known. The question as to whether the vaccine should be employed depends to a large extent upon the likelihood of exposure to infection. When exposure is likely it is advisable to repeat the vaccination annually. In areas in which the risk is large, the vaccine would be recommended especially for ranchers, campers and others, while in areas in which the disease is rare, vaccination hardly can be justified. The vaccine contains egg protein, hence should not be given to persons sensitive to egg protein.

Dosage.—0.5 cc. to 2.0 cc., depending on the age of the subject, to be repeated once or twice at intervals of from 5 to 10 days.

E. R. SQUIBB & SONS, NEW YORK

Rocky Mountain Spotted Fever Vaccine: 4 cc. vials. Preserved with sodium ethylmercurithiosalicylate 1:10,000.

PENICILLIN (See New and Nonofficial Remedies 1947, p. 144).

The following dosage forms have been accepted:

ELI LILLY & COMPANY, INDIANAPOLIS

Crystalline Penicillin G Potassium: 100,000, 200,000, 500,000 and 1,000,000 units, 20 cc. vials.

Ointment Crystalline Penicillin G Potassium: 1,000 units per gram, 28 Gm. tubes.

Ophthalmic Ointment Crystalline Penicillin G Potassium: 1,000 units per gram, 3.5 Gm. tubes.

Troches Crystalline Penicillin G Potassium: 5,000 units.

COMMERCIAL SOLVENTS CORP., NEW YORK

Crystalline Procaine Penicillin G in Oil: 300,000 units per cc., in peanut oil, 10 cc. vials.

MERTHIOLATE (See New and Nonofficial Remedies 1947, p. 96).

The following dosage form has been accepted:

ELI LILLY & COMPANY, INDIANAPOLIS

Ointment Merthiolate: 1:1,000, 28 Gm., 450 Gm. (1 lb.) and 2.26 Kg. (5 lbs.) jars. Merthiolate 0.1 per cent in a hydrophilic ointment base.

AMINOPHYLLINE-U. S. P. (See New and Nonofficial Remedies 1947, p. 305).

The following dosage form has been accepted:

ESTRO CHEMICAL CO., INC., NEW YORK

Solution Aminophylline: 0.25 Gm., 10 cc. ampuls; 0.5 Gm., 2 cc. and 20 cc. ampuls.

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SATURDAY, NOVEMBER 20, 1948

LYMPHOCYTES AND GLOBULIN

At a recent conference on lymph held by the New York Academy of Sciences, White and Dougherty [1] presented important statements on the newer knowledge of lymphocytes. The Yale investigators said that the structure and function of lymphoid tissue are controlled by pituitary-adrenal cortical secretion and that changes can be observed in this tissue following stimulation of the pituitary or the administration of adrenal cortical preparations. The changes are: a dissolution of lymphocytes in lymphoid structures, a profound lymphopenia, an increase in serum beta globulins and gamma globulin and, in the immunized animal, a release of antibody globulin to the circulation.

The dissolution of lymphocytes is characterized by a shedding or budding of the lymphocyte cytoplasm. As a consequence, this material is released to the lymph and, thus, to the systemic circulation. Lymphocytes, in the normal animal, contain a protein identical with the normal serum gamma globulin; a second component of lymphocytes is probably identical with the beta globulin of serum. Therefore, the accentuated cytoplasmic budding of lymphocytes, resulting from augmented adrenal cortical hormone concentration, causes an increased amount of lymphocyte globulins in the blood.

The increased dissolution rate of lymphocytes within lymphoid structures results in a failure of delivery of these cells to the circulation. The adrenal cortical steroids controlling lymphocyte dissolution are those which are oxygenated in position 11 of the steroid nucleus. Thus the peripheral lymphopenia following acute adrenal cortical stimulation is a readily determined manifestation of adrenal cortical activity. The presence of acute lymphopenia may be accepted as evidence that the sequence of events described is taking place.

Lymphocytes are the most widely distributed cells in the body. The release of the protein of lymphocytes following augmented pituitary–adrenal cortical secretion suggests that lymphocytes are a storehouse of readily available protein. This protein may be a significant portion of the reserve or deposit protein and the source of a large proportion of the extrahepatic nitrogen which appears in the urine in conditions of stress. Involution of lymphoid tissue and the loss of nitrogen from lymphoid tissue as a result of fasting occur only in the presence of intact adrenals. In the adrenalectomized animal, the reserve protein present in lymphocytes cannot be released during a period of fast. The availability of this protein in other circumstances of stress also probably depends on the presence of the pituitary and the adrenals.

An intimate relationship has been demonstrated between plasma globulins and lymphocyte proteins. The cytoplasmic proteins of lymphocytes and the hormonal control of their release attain added significance in the light of the various stimuli, including hemorrhage, chronic inanition, injection of heterologous protein or protein derivatives and irritation of the peritoneum, which activate the pituitary–adrenal cortical mechanism.

The demonstration of the high nutritive value of gamma globulin, a normal constituent of lymphocytes, adds importance to the role of these cells in protein metabolism. Indeed, the lymphocyte may bear a relationship to protein metabolism similar to that of the fat cell to lipid metabolism.

A portion of the protein of lymphocytes in the immunized animal is labeled globulin or antibody, and the rate of release of this protein is regulated by the same factors that control release of protein from lymphocytes in the nonimmunized animal. The demonstration of the basis of the anamnestic response is proof that lymphocytes are a storehouse of protein. Animals without circulating antibody have been shown to have antibody within their lymphocytes, and this labeled globulin is released to the circulation, as a result of increased supply of pituitary–adrenal cortical hormones. Increased secretion of the animal's own adrenotropic hormone may occur in response to a wide variety of stimuli which are known to activate pituitary–adrenal cortical secretion. Hemorrhage, cold, heat, bacterial toxins, foreign proteins and toxic chemical agents all activate the hormonal mechanism and have been used to demonstrate the anamnestic response. Several investigators have suggested that reticuloendothelial cells are concerned with the production of immune globulin.

As lymphocytes have been demonstrated to contain antibody, it is evident that, as these cells reproduce themselves, the labeled globulin constituent of the cytoplasm is transferred to the daughter cells. Tumors which developed from transplants of antibody-containing malignant lymphocytes were shown to contain as much immune globulin as the tumor from which the tissue was taken for transplantation. Therefore, factors which increase the number of lymphocytes will also augment production of antibody by increasing the available potential store of immune globulin.

1. White, A., and Dougherty, T. F.: Role of Lymphocytes in Normal and Immune Globulin Production, and the Mode of Release of Globulin from Lymphocytes, Ann. New York Acad. Sc. **46**: 859 (Sept.) 1946.

The presence of antibody in lymphocytes gives added significance to the wide distribution of these cells in the body. At least one major function of the lymphocytes which are infiltrating into all of the tissues of the body is, no doubt, to serve as a medium of distribution of gamma globulin. The recent demonstration of the high nutritive value of gamma globulin suggests that lymphocytes supply to cells throughout the body a protein which may fulfil nutritive and, perhaps, other physiologic needs of the body cells.

Some investigators have not been able to confirm the theory mentioned, particularly the part which relates to the dissolution of lymphocytes with the release of globulin antibodies. The differences in results attained by the various critics of this theory perhaps will stimulate further research on lymphocytes as well as antibodies, about which important subjects far too little is known.

DIABETES DUE TO ALLOXAN

Diabetes mellitus was first produced experimentally in dogs by von Mering and Minkowski in 1889 by means of total extirpation of the pancreas. G. F. Young in 1937 produced diabetes in dogs by daily injection of extracts of anterior pituitary for a period of several weeks. Dunn, Sheehan and McLetchie,[1] while attempting to elucidate the pathogenesis of the crush syndrome, administered alloxan to various animals in an effort to establish tubular nephritis. Many animals died during the first day. Investigation of these deaths revealed acute necrosis of the islet tissue of the pancreas. The development of this lesion was accompanied by an initial rise of the blood sugar, followed by intense hypoglycemia; they believed that the lesion was caused by overstimulation of the islets with overproduction of the insulin and later death of the cells by overstrain. Jacobs[2] first described the initial hyperglycemic and hypoglycemic phases following intravenous administration of alloxan in rabbits, and observed the symptomatic relief of the hypoglycemia by the administration of glucose. Later the phase of hyperglycemia was added to the picture.

The production of diabetes without nephritis is dependent on the difference between the nephrotoxic and diabetogenic doses. Early death following injection of alloxan could be prevented by prophylactic administration of glucose. When animals were thus sustained during the period of hypoglycemia, they survived and became permanently diabetic. Dunn and McLetchie, Baily and Baily, Goldner and Gomori and Houssay and his co-workers produced sustained diabetes due to alloxan in rats, rabbits, dogs, monkeys and cats. Diabetes due to alloxan, according to Lukens,[3] is a partial pancreatectomy produced by a chemical agent the effect of which is to cause selective degeneration of the beta cells. The subsequent diabetes may vary from the mildest to the most severe type. Diabetic animals respond readily to insulin. The diabetes may be controlled by the regular use of insulin. Large doses of alloxan produce severe diabetes and renal insufficiency terminating in acidosis and coma.

The most striking complication of diabetes due to alloxan in rats and rabbits has been the development of cataract. The incidence of cataract is greater and the appearance time shorter when diabetes is severe. In addition to cataract one group of investigators has reported the occurrence of retinal lesions consisting of capillary hemorrhages. Chestler and Tislowitz observed that immature rats with diabetes due to alloxan were strikingly dwarfed, some remained sexually infantile, and the intestinal tract was enlarged in proportion to body weight.

Pathologic studies of diabetes due to alloxan emphasize that injury from alloxan takes place within a few minutes of its injection and that the subsequent alterations are the consequence of this initial injury. The changes which begin immediately after the injection of alloxan progress to the complete disintegration of the beta cells within six hours, that is, at the onset of the hypoglycemic phase. The final picture after diabetes has existed for a few weeks is that of striking atrophy of the islands. The acinar tissue is usually normal. The toxicity of alloxan for the beta cells of the islands of Langerhans is accompanied by damage of the renal tubules. The thyroid, parathyroid and pituitary glands are usually described as normal. The liver has been reported by most observers as normal. Adrenal glands increase in weight in alloxan as in pancreatic diabetes.

Alloxan was first given to man by Brunschwig[4] and his co-workers to relieve hyperinsulinism due to islet cell carcinoma. They also gave it to 4 patients with severe malignant disease of other types. The 4 persons with normal blood sugar had a negligible hyperglycemic phase and no evidence of diabetes. Increasing amounts were given over periods up to six days. This experience suggested that man is resistant to alloxan. Conn[5] reported a case of a man with a pancreatic islet cell tumor and hyperinsulinism. The patient was given a nine day course of alloxan injections. At operation the tumor was found and removed. The islets of the pancreas proper were found to be severely damaged. Immediately on removal of the tumor typical diabetes mellitus developed. This experience suggests that the pancreatic islet tissue of human beings is sensitive to alloxan. Conn's experience contradicts the repeatedly expressed opinion that human islet tissue is exceedingly resistant to the degenerative effects of alloxan.

1. Dunn, J. S.; Sheehan, H. L., and McLetchie, N. G. B.: Necrosis of Islets of Langerhans Produced Experimentally, Lancet **1**: 484-487 (April 17) 1943. Dunn, J. S., and McLetchie, N. G. B.: Experimental Alloxan Diabetes in the Rat, ibid. **2**: 384-387 (Sept. 25) 1943.
2. Jacobs, H. R.: Hypoglycemic Action of Alloxan, Proc. Soc. Exper. Biol. & Med. **37**: 407-409 (Nov.) 1937.
3. Lukens, F. D. W.: Alloxan Diabetes, Physiol. Rev. **28**: 304-330 (July) 1948.
4. Brunschwig, A.; Allen, J. G.; Owens, F. M., Jr., and Thornton, T. F.: Alloxan in the Treatment of Insulin Producing Islet Cell Carcinoma of Pancreas, J. A. M. A. **124**: 212-216 (Jan. 22) 1944.
5. Conn, J. W., in discussion on Bailey, C. C.; Bailey, O. T., and Leech, R.: Alloxan Diabetes, Proc. Am. Diabetes A. (1946) **6**: 375-393, 1947.

Present evidence indicates that the action of alloxan on the islands of Langerhans is exerted directly. The pathologic changes are believed to be the consequences of an immediate toxic injury of the beta cells. The initial hyperglycemic phase has been prevented by insulin, phlorizin, adrenalectomy, hypophysectomy and hepatectomy. The most generally accepted hypothesis, according to Lukens, is that preformed insulin is liberated from the damaged islets. Diabetes due to alloxan is a valuable aid in the study of diabetes. Evidence does not indicate that alloxan is related to human diabetes mellitus.

UNDERSTANDING PEOPLE

Science during the next century, said Roger J. Williams, addressing the Centennial Meeting of the American Association for the Advancement of Science, will predominantly be occupied with human science. Physical sciences and their applications will continue to thrive, but the most significant development of the next century, he believes, will be in the realm of human science or of understanding people. Social problems can be solved only if we understand what people are like. Human beings, Williams believes, should be studied anatomically, physiologically, psychologically and in their social relations. Differentiation or individuality is a potent factor in every social problem. One of the crucial tests in understanding people is to know how they are alike and how they differ from one another. Probably inequalities are the very basis of our democracy. If we were all the same and had the same likes and dislikes, there would be no need for freedom. We would all fall readily into the same pattern of life, and difficulties would never arise. Because we do have individuality we want freedom to make our own decisions and live our own lives.

People differ one from another because of their inheritance and because of the differences in environmental influences. The relative importance of the two factors is a matter of conjecture and opinion. Inherent individuality is most highly developed in man. Superimposed on these inherent differences are differences induced by environmental and cultural influences.

People differ in the size and shape of their bodies and their heads, noses, hands, feet and legs. Individuality in shape, size and cellular composition are just as pronounced with respect to our thyroids, our adrenals, our sex glands and our pituitary glands. It is, therefore, not surprising that we do not always see eye to eye and that our other senses do not work uniformly for all of us. Williams cites an experiment in which a chemical was tested in a special study of 6,377 persons. Of those who tested it 21.3 per cent found it tasteless, 64.5 per cent found it bitter, many extremely so, 5.4 per cent found it sour, 2.1 per cent found it sweet, 4.8 per cent found it salty and the remaining 1.9 per cent ascribed to it miscellaneous other tastes.

The work of Beadle and his associates demonstrated that people inherit through the agency of genes their entire metabolic machinery, and, since each inheritance is distinctive, it follows that everyone has metabolic machinery that is distinctive. The most apparent outward manifestation of the existence of distinctive metabolic patterns is the existence of allergies and differences in the responses to drugs.

Williams also stresses that intelligence is not a unitary trait possessed in high degree by some and in low degree by others. There are many different ways in which one can be intelligent. The most compelling evidence of this fact is the existence of the so-called idiot-savants. Williams feels that the greatest benefits to be derived from a revised school system will come from recognition and care for individuality. The schools of the future will devote considerable effort in the earliest grades to helping the students to become acquainted with themselves.

Current Comment

ATOMIC ENERGY COMMISSION FELLOWSHIPS

The Atomic Energy Commission has established a fellowship program for physicians who desire to be trained and carry on research in the field of atomic energy as it relates to medicine. The Commission requested the National Research Council to undertake the administrative responsibilities of the fellowship program. A committee has been established in the Council which considers applications from physicians under 35 years of age who have had one year internship or equivalent training. The fellowships, which are for one year, may be renewed. The candidate is expected to enroll in nuclear radiation physics, pertinent mathematics and certain courses in chemistry. He may make arrangements for this instruction and, if that is not feasible, may attend one of the regional training centers which have been established by the Atomic Energy Commission. This basic training will comprise lectures, laboratory exercises and demonstrations for about six months, after which fellows will have an opportunity to participate in research projects which the Atomic Energy Commission is supporting at various institutions throughout the United States. Fellows will be able to maintain contact with clinical medicine through the affiliated medical schools and hospitals. The Commission has released the names of forty-four fellowships recently awarded under this program. Five classes of research fellowships have been established, including not only medical science but physical, biologic and agricultural sciences as well. The postdoctoral fellowships carry a basic stipend of $3,000 a year, the predoctoral a basic stipend of $1,600 a year, and these may be increased to provide for support of dependents or other special needs of the fellows. The Atomic Energy Commission considers this program an integral part of its activities. There is a shortage of scientific personnel in medical and allied fields as they relate to atomic energy.

ORGANIZATION SECTION

Official Notes

SCIENTIFIC EXHIBIT—ATLANTIC CITY SESSION

The Scientific Exhibit will mark its Fiftieth Anniversary at the Atlantic City Session, June 6-10, 1949. This feature of the meeting was started in 1899 as a pathology exhibit, and in 1903 was expanded to include all branches of medicine. Awards for the best exhibits have been made since 1908.

At the coming meeting in Atlantic City, each of the eighteen Sections of the Scientific Assembly will sponsor a group of exhibits. Final selection of exhibits and assignment of space will be made after all applications have been received by the Committee on Scientific Exhibit of the Board of Trustees, consisting of Dr. Dwight H. Murray, Napa, Calif.; Dr. E. J. McCormick, Toledo, Ohio, and Dr. Gunnar Gundersen, LaCrosse, Wis.

Application blanks for space in the Scientific Exhibit at Atlantic City are now available and may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10, Ill.

COUNCIL ON NATIONAL EMERGENCY MEDICAL SERVICE

The American Medical Association's Council on National Emergency Medical Service held its third regular meeting in Chicago, November 1. This agency of the Board of Trustees, established in 1947, is dedicated to a continuous study of the medical, health and sanitary needs of the nation's armed forces, industry, agriculture and the civilian population at large in time of national stress, disaster and emergency.

In attendance were Dr. Roscoe L. Sensenich, President of the Association; Dr. Elmer L. Henderson, Chairman of the Board of Trustees; Dr. Morris Fishbein, Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION; Dr. James E. Paullin and Dr. Edward L. Bortz, both former Presidents of the Association, and Dr. James C. Sargent, Chairman of the Council. In addition to the Council members and consultants, approximately twenty-five other physicians, including Council secretaries and Bureau directors of the Association, were present. Dr. Carl Peterson, Secretary of the Council on Industrial Health, reported that in the event of another war the success of an industrial health program now universally recognized as a vital factor in defense would largely depend on the complete coordination of military and civil work. Appropriate steps, he disclosed, have already been undertaken to assure a comprehensive plan to meet the emergency. Dr. James R. Wilson, Secretary of the Council on Foods and Nutrition, reported briefly on the subject of nutritional aspects of national security. Dr. Donald G. Anderson, Secretary of the Council on Medical Education and Hospitals, analyzed the medical graduate training program now in operation by the Armed Forces. Mr. Edwin Holman, representing Mr. J. W. Holloway Jr., Director of the Association's Bureau of Legal Medicine and Legislation, reported on legal aspects of legislation in connection with the Selective Service Act.

The Council, mindful of its responsibilities to the profession and the public at large and giving heed to the threat of atomic warfare, took cognizance of the fact that certain of its basic recommendations require reiteration by the Association. With the view in mind of placing increased emphasis on the medical phase of planning for national defense, it was recommended that the Board of Trustees reintroduce the following resolutions to the House of Delegates:

Be it Resolved, "That the President of the United States of America and the Congress be respectfully urged:

"That in peace as in time of war the Surgeon General of the Army, the Surgeon General of the Department of the Navy and the Air Surgeon, Department of the Air Force, have the authority and responsibility for participation, with commensurate rank and at the level of the Chiefs of Staff and the Chiefs of Naval Operations of the Armed Forces, in all military and naval planning, organization and operations as these relate to medical, health, sanitary and welfare services and for the assignment and utilization of medical and allied personnel at home and abroad."

Be it Resolved, "That the American Medical Association, by action of its House of Delegates, desires to assure the highest type of professional care for the members of the Armed Forces. It is imperative that a permanent 'Civilian Medical Advisory Board' be established by the Secretary of Defense with the least possible delay. This 'Civilian Medical Advisory Board' to be composed of doctors of medicine, appointed from civilian life by the Secretary of Defense and responsible under policies established by him for the development of all medical policies, procedures and programs required by the medical and hospital services of the Armed Forces and to affect the utmost coordinated efforts between the several departments, boards and agencies of the Armed Forces."

In addition, the Council, with the view in mind of being helpful to the Armed Forces in the solution of their present medical personnel problem, recommends that the Board of Trustees introduce the following proposed resolution to the House of Delegates:

Be it Resolved, "That in the light of current medical personnel shortages, and in line with the accepted policy for coordination by the Armed Forces, every effort should be made to consolidate the facilities for the hospital care of the several Armed Forces.

"That the patient load in military hospitals, particularly of non-military patients, be reduced to the minimum consistent with the primary mission of the Armed Forces as defined by Congressional Acts."

Washington Letter

(From a Special Correspondent)

Nov. 11, 1948.

All 7 Physician Representatives Returned to Congress

The radical change in the complexion of the House of Representatives which was produced by the national elections did not remove any of the seven incumbents who are doctors of medicine. All were reelected. They are: (Republicans) Drs. Ivor D. Fenton, Pennsylvania; Walter Judd, Minnesota; A. L. Miller, Nebraska, and Frederick C. Smith, Ohio; (Democrats) E. H. Hedrick, West Virginia; Thomas E. Morgan, Pennsylvania, and Joseph L. Pfeifer, New York.

Oddly enough, none of the physician members of Congress is a member of the House Interstate and Foreign Commerce Committee, which handles virtually all proposed legislation pertaining to medical research and health economics. It is this committee which, in the 81st Congress, will hold hearings on national health insurance, expansion of the U. S. Public Health Service, extension of child health activities by the federal government, amendment of the Hill-Burton hospital construction law, food and drug legislation and modification of federal cancer and venereal disease control statutes.

However, with the Interstate and Foreign Commerce Committee due to be reorganized and many new faces added as a result of the election, it is not improbable that at least one

physician will join its membership. Five of its Republican members were defeated. Three of its Democrats are gone, one by retirement, one by defeat at the polls and one by promotion to the Senate (Chapman, Kentucky). This means that eight Democrats and, in event of committee reassignments, one or more Republicans will be appointed to the committee.

Senator Murray Will Head Health Subcommittee

Reorganization of the Senate in January will make Senator James E. Murray (Democrat) of Montana chairman of the health subcommittee of the Senate's Committee on Labor and Public Welfare. Chairman of the full committee will be Senator Elbert D. Thomas (Democrat) of Utah. The reorganized health subcommittee, which will handle the bulk of medical and public health legislation to be considered by the Senate—including federal health insurance bills—probably will be composed of Murray, Pepper and Hill, Democrats, and Smith and Donnell, Republicans. Ball of Minnesota is the only member of this committee who was an election casualty.

McCarran and Rooney Due to Become Chairmen

Prospective chairman of the Senate Appropriations Subcommittee which will be in charge of the annual budget for the Federal Security Agency (which includes the U. S. Public Health Service, the Food and Drug Administration and the Social Security Administration) is Senator Pat McCarran (Democrat) of Nevada. He will replace the Republican incumbent, Senator William F. Knowland, of California. His "opposite number" in the House is expected to be Representative John J. Rooney (Democrat) of New York, who would replace Representative Frank B. Keefe (Republican) of Wisconsin.

Other committees, chiefly Labor and Public Welfare in the Senate and Interstate and Foreign Commerce in the House, are responsible for enabling legislation on federal participation in public health, subsidization of professional education, medical research and related programs. But it is the respective appropriations committees which hold the power on the amount of money that shall be expended on them.

Military Research Group on Field Inspection Trip

Accompanied by Army, Navy and Air Force staff assistants, members of the Research and Development Board's medical sciences committee departed October 26 for a ten-day air tour of military medical research facilities in North Carolina, Florida, Louisiana, Texas and Kentucky. Dr. Francis G. Blake, committee chairman, headed the party. Other members included Drs. Joseph F. Sadusk Jr., executive secretary, Lowell T. Coggeshall, John S. Lockwood, Wallace O. Fenn, James E. McCormack and William H. Fitzpatrick. Among those in the military contingent were Brig. Gen. George E. Armstrong, Deputy Surgeon General of the Army; Capt. W. P. Dana, head of the research division in the Bureau of Medicine and Surgery, Navy Department, and Brig. Gen. John M. Hargreaves, Deputy Air Surgeon. Installations which the group was scheduled to visit included the Naval Medical Research Laboratory at Camp Lejeune, N. C.; Orlando, Fla., entomologic laboratories of the Department of Agriculture; the Naval School of Aviation Medicine at Pensacola, Fla.; Randolph Field School of Aviation Medicine; Army Medical Field Research Laboratory at Fort Knox, Ky., and Eglin Field, Fla.

Nearly $1,000,000 in Research Grants Approved by Federal Council

A total of ninety-four medical research grants, aggregating $931,605, has been approved by the National Advisory Health Council, according to a tabulation obtained from the Division of Research Grants and Fellowships, National Institutes of Health. Favorable action on the applications, comprising thirty-eight continuation grants and fifty-six new projects, was taken at the October 22-23 meeting of the advisory council.

Tuberculosis received the largest share of the allocations—seven projects totaling $128,865. Investigations on metabolism and endocrinology ranked second, with $113,222 for sixteen separate investigations. Next in order were pathology, $81,390; physiology, $75,137, and biochemistry and nutrition, $69,437. Lesser amounts were approved for investigations in antibiotics, bacteriology, cardiovascular diseases, dental problems, gerontology, hematology, pharmacology, public health methods, radiobiology, sanitation, surgery, syphilis, tropical disease and virus and rickettsial infections.

Of the twenty fields of research with which the National Advisory Health Council is concerned, only one—malaria—was not represented by an award. Recipients of the grants will be announced later by the U. S. Public Health Service.

$455,715 in Federal Medical Research Grants Approved

Thirty-seven grants, totaling $455,715, for research in medical and related fields have been approved by the U. S. Public Health Service, on recommendation of the National Advisory Health Council. Recipient of the largest award, $64,620, was Dr. Esmond R. Long, for investigations in streptomycin therapy of tuberculosis. Among other recipients were Northwestern University Medical School, $48,000, for research in rheumatic fever; Duke University, $30,326, for work on relationship between diet and hypertensive vascular and renal diseases; Western Reserve, $27,884, for revascularization of the heart, and New York University, $27,985, for research in biologic aspects of schistosomiasis.

Next meeting of the National Advisory Health Council will be on February 18. Applications for research grants, to be considered at this meeting, must be received no later than December 1 by the National Institutes of Health (Division of Research Grants and Fellowships), Bethesda, Md.

Dr. Andrews Leaves on Special Malaria Mission to Iran

His mission reflecting the importance attached by the federal government to fostering of friendly relations with the Middle East, Dr. Justin Andrews left Washington late in October to lay the groundwork for an intensive malaria eradication program in Iran. According to the State Department, his services were requested by the Iranian government, which is anxious over extremely high incidence of malaria in the Azerbaijan region.

Dr. Andrews is head of the scientific section of the Communicable Disease Center operated by the U. S. Public Health Service at Atlanta, Ga. During World War II he served in the Army as a malariologist, first in the Mediterranean area and later in the Southwest Pacific.

Coming Medical Meetings

American Medical Association Interim Session, St. Louis, Municipal Auditorium, Nov. 30-Dec. 3. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Annual Conference of State Secretaries and Editors, St. Louis, Hotel Statler, Nov. 28-29. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

National Medical Public Relations Conference, St. Louis, Hotel Statler, Nov. 27. Mr. Lawrence W. Rember, 535 N. Dearborn St., Chicago 10, Director.

American Academy of Dermatology and Syphilology, Chicago, Palmer House, Dec. 5-9. Dr. Earl D. Osborne, 471 Delaware Ave., Buffalo, Secretary.

American Academy of Pediatrics, Atlantic City, Chalfonte-Haddon Hall, Nov. 20-23. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Society of Tropical Medicine, New Orleans, Roosevelt Hotel, Dec. 5-9. Dr. Frederick J. Brady, National Institute of Health, Bethesda 14, Maryland, Secretary.

Association for Research in Nervous and Mental Diseases, New York, Waldorf-Astoria Hotel, Dec. 10-11. Dr. Clarence C. Hare, 700 W. 168th St., New York 32, Secretary.

Eastern Section, American Federation for Clinical Research, Philadelphia, Temple University School of Medicine, Dec. 4. Dr. J. Edward Berk, Temple University School of Medicine, Philadelphia, Chairman.

Puerto Rico, Medical Association of, Santurce, Dec. 10-12. Dr. J. Basora Deñllo, Box 3866, Santurce, Secretary.

Radiological Society of North America, San Francisco, Dec. 5-10. Dr. Donald S Childs, 607 Medical Arts Bldg., Syracuse 2, N. Y., Secretary.

Southern Psychiatric Association, Dallas, Texas, Hotel Adolphus, Dec. 6-7. Dr. Newdigate M. Owensby, 384 Peachtree St. N.E., Atlanta, Ga., Secretary.

Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 7-9. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Western Surgical Association, St. Louis, Dec. 2-4. Dr. Warren H. Cole, 1853 W. Polk St., Chicago 12, Secretary.

GOVERNMENT SERVICES

ARMY

COMMITTEE ON CHEMICAL WARFARE

The Research and Development Board of the National Military Establishment announces the appointment of Dr. W. Albert Noyes Jr., professor of chemistry, University of Rochester, as chairman of the recently established Committee on Chemical Warfare. The Committee will work with the Office of Civilian Defense Planning, National Military Establishment. Professor Arthur C. Cope, chairman, department of chemistry, Massachusetts Institute of Technology, has been appointed alternate to Dr. Noyes; others on the Committee are H. F. Johnstone, professor of chemical engineering, University of Illinois, with A. P. Colburn, University of Delaware, as his alternate; and Robert C. Swain, Vice President of the American Cyanamide Company, with R. T. Major, Vice President of Merck and Company, as his alternate. In addition to those named, members from the three military departments will serve on the Committee, the acting executive director of which is H. I. Cole, Ph.D., who served with the Chemical Warfare Service in World War I and in the Chemical Corps, U. S. Army, in World War II.

TRAINING IN CIVILIAN INSTITUTIONS

The following medical department officers have been accepted for training in the civilian institutions indicated: Colonel Charles J. Farinacci, Cornell University, cytologic diagnosis of cancer; Lieutenant Horace W. Shreck, Bellevue Hospital, New York, ophthalmology; Captain Charles I. Hamilton Jr., Franklin Hospital, San Francisco, clinical medicine; and for intern training as first lieutenants Sidney L. Brown, San Francisco City and County Hospital; Joseph C. Cullina, Gallinger Municipal Hospital, Washington, D. C.; Jack D. Fetzer, Hermann Hospital, Houston, Texas; John M. Kohl, Wilkes-Barre General Hospital, Wilkes-Barre, Pa.; Alfred Lubart, Morrisania City Hospital, New York; Tom E. Nesbitt, University Hospital, Ann Arbor, Mich.; John Thomas Olive, St. Joseph's Hospital, Kansas City, Mo., and Robert G. Richards, White Memorial Hospital, Los Angeles.

EXHIBIT AT CENTENNIAL CELEBRATION

At the Centennial Celebration of the establishment of Fort Bliss at El Paso, Texas, November 3-7, the Army Medical Illustration Service of the Army Institute of Pathology presented an exhibit made up of thirteen panels, one of which was a photomontage of "The Healthiest Soldier in the World." Five other panels supported the theme by showing how a recruit gains through preventive medicine, expert medical attention and Army service, and how the country profits from Army research and the Army training program for medical personnel. In the center of the exhibit a section was devoted to William Beaumont, an Army medical officer and America's first experimental physiologist, whose observations on the Canadian trapper Alexis St. Martin led to the modern studies on digestion and dietetics.

NAVY

COURSE IN AVIATION MEDICINE

Regular and reserve medical officers up to and including the rank of lieutenant commander may make application for the next course in aviation medicine to be held at the school of Aviation Medicine and Research, Pensacola, Fla., beginning Jan. 17, 1949. Instruction will be given in such subjects applicable to aviation medicine as cardiology, ophthalmology, otolaryngology and applied aviation physiology. Students will then be assigned to flight indoctrinal training and ground school work, after which successful students will be designated Naval flight surgeons. Applications must reach the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., prior to Dec. 10, 1948.

NEW NAVY INTERNS

The following recent graduates have accepted commissions as lieutenants (jg) in the Medical Corps Reserve for internship in civilian institutions under the Navy Medical Intern training Program: George F. Batten, Chelsea, Mass., to the Naval Hospital, Bethesda, Md.; Robert M. Clark, Canton, Ohio, to Mercy Hospital in that city; Leonard O. Congit, Los Angeles, to Queen of Angels Hospital in that city; Robert W. Hoellwarth, Lodi, Calif., to DePaul Hospital, St. Louis; Harold D. Lankford, St. Louis, to St. Louis City Hospital; Joseph J. Miller, Reinerton, Pa., to Reading Hospital, Reading, Pa.; David P. Morris Jr., Detroit, to Harper Hospital, Detroit; Eugene R. Odou, Los Angeles, to Los Angeles County Hospital in that city; David J. Seel, Bradenton, Fla., to Charity Hospital, New Orleans; Jack D. Stringham, Salt Lake City, to Latter Day Saints Hospital in that city; Robert B. Tator, New Haven, Conn., to Baylor University Hospital, Dallas, Texas; Wyman C. Tremblay, Hollywood, Calif., to Queen of Angels Hospital in Los Angeles; Mark M. Walter Jr., Lansdowne, Pa., to Philadelphia General Hospital, and Francis P. Weyrens, Hebron, N. D., to St. Mary's Group Hospitals, St. Louis.

OFFICERS REQUEST ACTIVE DUTY

The following reserve medical officers have requested active duty in the Navy: Comdr. William M. Cason, Atlanta, Ga.; Lieut. Comdr. Ulysses S. Geiger, North English, Iowa; Lieut. Charles E. Weber, Rochester, N. Y., and Lieutenants (jg) Victor G. Benson, Soldiers Grove, Wis., and Jerome Imburg, Richmond, Va.

PUBLIC HEALTH SERVICE

CLEARINGHOUSE FOR CHILD LIFE RESEARCH

The Children's Bureau in Washington, D. C., has established a clearinghouse for research in child life in response to numerous requests for a center that would promote interchange of information on current research in fields affecting child life. The clearinghouse will contact investigators for reports of studies in progress. It will not attempt to summarize or indicate the conclusions of research projects but will furnish accounts of the nature of the projects as reported by individuals and organizations. The clearinghouse grew out of a series of conferences held to review what is going on in research in child life. Further information may be obtained from Clara E. Councell, Director, Clearinghouse, Children's Bureau, Washington 25, D. C.

DR. EAGLE RETURNING FROM AFRICA

Dr. Harry Eagle, chief, research branch, National Cancer Institute, is returning from Africa where for several weeks he studied the effects of using arsenical compounds for sleeping sickness, a treatment which he helped develop in 1944-1945. Use of para-arsenosophenylbutyric acid for trypanosomiasis was developed by Dr. Eagle in collaboration with the Sleeping Sickness Services of the Belgian Congo, French Equatorial Africa, French West Africa, the Gold Coast, Nigeria, and the Firestone Plantation in Liberia. At that time Dr. Eagle was head of the U. S. Public Health Service Venereal Disease Research and Postgraduate Training Center located at Johns Hopkins Hospital, Baltimore. An account of this work appears in *Public Health Reports*, July 12, 1946, page 1019.

MEETING OF QUARANTINE OFFICERS

All medical officers in charge of the major quarantine stations of the Public Health Service, those in charge of medical examinations of visa applicants in Europe and Montreal, and representatives of the nonmedical quarantine inspection officers and sanitary inspectors held their first meeting in Washington September 20-24. The conference agreed on standard measures to modernize quarantine further to meet the demands of international commerce while still affording adequate protection against importation of disease. They voted unanimously to retain the present smallpox immunization requirements and to continue the rabies control work. Technical information was furnished by representatives of several organizations with work related to that of the Foreign Quarantine Division. The chief of the Canadian Quarantine and Immigration Medical Service was present as an observer and collaborator.

DR. DOULL TO DIRECT LEPROSY RESEARCH

The Federal Security Administrator announces that Dr. James A. Doull, chief, Office of International Health Relations, Public Health Service, has been detailed to the American Leprosy Foundation (Leonard Wood Memorial) as Director of Research with headquarters in Washington. Studies will be made on the epidemiology of leprosy and methods of treatment. The Foundation is now supporting epidemiologic studies in the Philippines and a special bacteriologic laboratory at Harvard Medical School. Dr. Doull was chairman of the medical advisory board, American Leprosy Foundation from 1940 to 1943. He formerly was a professor at Western Reserve University School of Medicine, and served as medical consultant to UNRRA and the Foreign Economic Administration. He joined the Public Health Service in 1943.

Dr. L. L. Williams Jr., medical director, will succeed Dr. Doull as chief, Office of International Health Relations. He has for twenty-six years been a specialist in malaria control research. He was head of the malaria commission to the China-Burma Highway and at the start of the war organized malaria control in areas of camps and war industries. Detailed to the Army, he was a malariologist in the North African Theater of Operations.

REGULAR CORPS APPOINTMENT AS SANITARIAN

Examinations for appointment in the Regular Corps in the grades of assistant sanitarian and senior assistant sanitarian will be held in the near future. An applicant for the assistant grade must be a citizen of the United States at least 21 years of age, have a bachelor's degree from a school of recognized standing, in one or more fields which are related to milk and food sanitation, have a master's degree from an approved school in public health or in a related science, and have had at least seven years of educational (exclusive of high school) and professional training and experience. An applicant for the senior assistant grade in addition must have had at least ten years of educational (exclusive of high school) and professional training and experience.

The written examination for both grades will be in bacteriology, chemistry, physics, epidemiology, administration and their relation to environmental sanitation in general and to milk and food control in particular. Information may be obtained from the Surgeon General, United States Public Health Service, Washington 25, D. C.

MISCELLANEOUS

NINETEEN ATOMIC RESEARCH PROJECTS

The Atomic Energy Commission has selected nineteen research projects in biology and medicine proposed by nongovernmental institutions in ten states for financial support. These are in addition to thirty-eight projects announced last May by the Commission. Following is a list of the institutions in which this research will be conducted, the subject of the research, and the director of the project:

COLORADO

University of Colorado, Boulder
John R. Lacher—Study of Relationships Between Chemical Structure, Physical Characteristics and Biologic Activity in the Intermediate Metabolism of Nucleic Acid Derivatives
Theodore T. Puck—Study of the Radiation Chemistry of Bacteriophage Invasion and Reproduction in Host Cells

ILLINOIS

Northwestern University, Evanston
J. Roscoe Miller—Establishment of a Radioisotopic Unit for Instruction, Research and Therapy

MASSACHUSETTS

Massachusetts Institute of Technology, Cambridge
Robley D. Evans—Radiomedicine Research
Arnold Arboretum, Harvard University, Boston
Karl Sax—Dosage Curve Under Varying Conditions of Time and Intensity of Radiation

NEW YORK

College of Physicians & Surgeons, Columbia University, New York
David Nachmonsohn—Effects of Exposure to Radioactive Materials and to X-Ray Irradiation on Nerve Tissue
N. Y. Post Graduate Hospital, New York
Marion B. Sulzberger—Skin Changes Produced by Low-Voltage Roentgen Ray Irradiation

NORTH CAROLINA

N. C. University, Chapel Hill
H. D. Bruner—Measurement of Volume of Flow of Blood in the Kidney and Level of an Unanesthetized Man by Means of Radioisotopic Procedure

OHIO

Ohio State University, Columbus
J. L. Morton—Establishment of Physical and Medical Principles in Use of Artificially Radioactive Cobalt 60 for Treatment of Cancer
Western Reserve University, Cleveland
H. L. Friedell—Medical and Biologic Research on Toxicologic Effects of Thorium and the Comparative Effects of Various Types of Internally Distributed Ionizing Particles
Harland G. Wood—Intermediary Metabolism on Carbohydrates by Bacteria

OREGON

University of Oregon, Eugene
Arnold L. Soderwall and Paul Risley—Localization of Radioactive Isotopes in Reproductive and Germinal Tissues During Periods of Quiescence and Activation
Oregon State College, Corvallis
Joseph S. Butts—Mode of Action of 2-4-Dichlorophenoxyacetic Acid as Studied with the Use of C-14
V. H. Cheldelin and B. E. Christensen—Study of Vitamin-Amino Acid and Carbohydrate-Amino Acid Relationships Using C-14 as a Tracer Substance
University of Oregon Medical School, Portland
Edward S. West—Degradation of Radioactive Cholesterol Fatty Acids and Ketone Bodies in the Animal Body

TEXAS

Baylor University, Waco
Joseph H. Gast—Chemistry and Metabolism of Some Sulfur Oxides
University of Texas, Austin
Jack Myers—Biologic Accumulation of Inorganic Materials by Algae

WASHINGTON

University of Washington Medical School, Seattle
Robert H. Williams—Biologic Effects of Radioactive Sulphur

WISCONSIN

University of Wisconsin Medical School, Madison
James A. Miller—Labeled Azo Dye Research

These projects will be administered by the Office of Naval Research under the joint program of support of fundamental scientific research.

ASSIGN ATOMIC ENERGY FELLOWS

Nine medical officers from the armed forces, one from the Public Health Service, and one from the British Royal Navy have been assigned to training centers for study under the Atomic Energy Commission fellowship program. The centers to which these officers have been assigned for six months are at the University of Colorado, Denver; Duke University, Durham, N. C., and Reed College, Portland, Ore. Following this six months' course in basic training, the fellows from the armed forces and Public Health Service are expected to be assigned to Atomic Energy Commission installations for field training. The medical officers assigned are as follows: Captain Donald E. Dement, U.S.N.; Captain Paul M. Hoot, U.S.N.; Surgeon Commander Dennis A. Hovenden, British Royal Navy; Lieut. Col. Clinton C. Maupin, U.S.A.; Lieut. Col. John H. Rust, U.S.A.; Lieut. Comdr. Elmer R. King, U.S.N.; Lieut. Comdr. Peter S. Kwiatkowski, U.S.N.; Capt. Edward A. Langdon, U.S.A.; Lieut. (jg) Garner L. Lewis, U.S.N.; First Lieut. Ellis Oster, U.S.A.; Dr. Samuel C. Ingraham, Surgeon, U. S. Public Health Service.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Brock, Jack.....New Brockton
Clayton, Orville W.....Fort Payne
Fargason, Crayton C. Jr.....Dadeville
Hanks, Boyce L.....Monroe
Kennamer, Samuel R.....Montgomery
Lamb, Robert H.....Troy
Mason, Robert H.....Russellville
Nabers, Hugh C.....Birmingham

Arkansas

Bell, Henry Grady Jr.....Little Rock
Birdsong, Karl K.....Shiloh
Brogdon, Paul P. Jr.....Springdale
Clardy, Edgar K.....Hot Springs
Dicksinson, Rodger C.....Horatio
Leidinger, Karl J. Jr.....Monticello
Regnier, George G.....Parkdale
Scruggs, Joe Bartie Jr.....Little Rock
Silverblatt, Charles W.....Osceola

California

Aagaard, Carl M. J.....San Francisco
Connor, Harold L.....San Francisco
Jonte, Donald M.....Stockton
Kay, Fred M.....W. Los Angeles
Kempe, Charles H.....San Francisco
Kennedy, Dean M. Jr.....Beverly Hills
Latta, Harrison.....Los Angeles
Lauder, Clark H. Jr.....Arcadia
Leavitt, Lewis A.....Manhattan Beach
Pedersen, Frank A.....Los Angeles
Pitcairn, Donald M.....San Francisco
Rickabaugh, Donald E.....San Gabriel
Scheppler, George C.....Sanitarium
Smith, Lloyd E. Jr.....Los Gatos
Wilson, Austin R.....Yucaipa

Colorado

Atkins, Dale M.....Boulder
Cowen, Homer C.....Salida
Lubchenco, Michael A.....Sterling
Philpott, James A. Jr.....Denver
Wheeler, Gordon M.....Denver

Connecticut

Andy, Orlando J.....New Britain
Keefe, Arthur T. Jr.....New London
Winternitz, William W.....New Haven

Delaware

Cordrey, Lee J.....Laurel

District of Columbia

Alper, Melvin G.....Washington
Carter, John P.....Washington
Dun, Alan Andrews.....Washington
Hollander, Edward E.....Washington
Wilmer, John G.....Washington

Illinois

Carton, Robert W.....Lake Forest
Couri, Peter J.....Peoria
Cunningham, Clement P.....Rock Island
Dawson, Dwight Casner.....Riverside
Douglas, Donald B. Jr.....Lake Forest
Duncan, Robert J.....LaSalle
Frederick, Laurence D. Jr.....Chicago
Friedman, Irving A.....Chicago
Goldman, Leo M.....Chicago
Green, Maurice R.....Chicago
Heck, Charles Voisin.....Collinsville
Heifetz, Milton D.....Chicago
Hesselschwerdt, Gernon P.....Urbana
Katz, Irving A.....Chicago
Kutsunis, Harry T.....East Moline
Levinson, Julian D.....Chicago
McDonald, James E.....Oak Park
Matlavish, Richard T.....Christopher
Milewski, Stanley A.....Chicago
Mrazek, Rudolph G. Jr.....Chicago
Powers, William H.....Oak Park
Reis, Frederick M.....Chicago
Stewart, Homer E.....Hoopeston
Tuthill, Sanford W.....Mt. Vernon
Wilner, Warren K. Jr.....Chicago
Wright, John L.....Bloomington
Young, Robert L.....Chicago
Zdenek, Albert N.....Berwyn

Kansas

Gray, Charles L. II.....Topeka
Lockard, Vernon M.....St. Francis
Martin, Jack N.....Topeka
Stitt, Ronald W.....Dodge City

Kentucky

Gittleman, Isaac W.....Louisville
Hopkins, Scovell M.....Ashland
Kinnaird, David W.....Lancaster
Moore, Clyde T.....Buechel
Smith, Robert C.....Covington
Upchurch, Dorris L.....Capito
Woodson, Hylan H. Jr.....Eddyville

Louisiana

Knight, Edward H.....New Orleans
McHenry, Armand G. Jr.....Monroe
Scott, Samuel M.....Oakdale

Massachusetts

Bonner, Joseph N.....Boston
Calkins, Evan.....Newton
Carlisle, John C.....Boston
Fitzpatrick, Thomas B.....Brookline
Johnson, Robert M.....Haverhill
Keeler, Robert W.....Attleboro
Klein, Elihu I.....Pittsfield
Mack, Francis X.....Milton
Mackler, Edward D.....New Bedford
Parsons, Thomas C.....Boston
Rogan, Francis J.....Brighton
Roy, Joseph L.....Webster
Sudbay, James A. Jr.....Gloucester

Michigan

Bower, Donald W.....Detroit
Groat, Frank L.....Detroit
Hasegawa, Masato M.....Detroit
Hooper, Charles H.....Detroit
Kopp, Robert E.....Detroit
Kuipers, Siebe W.....Detroit
Lyttle, Sydney N.....Flint
McKeever, George E.....Detroit
Markey, Frank R.....Detroit
May, Donald G.....Detroit
Miller, Arthur A.....Detroit
Ritter, George.....Detroit
Sokol, William M.....Detroit
Stillwater, Karl.....Detroit

Minnesota

Burke, Edmund C.....Minneapolis
Halliday, Phillip V.....Virginia
Johnson, Herbert W.....St. Paul
Krawczyk, Henry J.....Minneapolis
Lerner, Aaron.....Minneapolis
Nimlos, Kenneth O.....Stephen
Rozycki, Anthony T. Jr.....Blackduck
Thayer, Merrill H.....Minneapolis
Yaeger, John J.....Sanborn

Mississippi

Brocato, Simone.....Merigold
Gruich, Frank G.....Biloxi
Hesdorffer, Eugene.....Canton
Mayfield, William B.....McComb
Wyatt, Sparkman H.....Lula

New York

Aquilina, Anthony M.....Buffalo
Auchincloss, Joseph H. Jr.....New York
Bergendahl, Emil Henry.....Manhasset
Berstein, Theodore.....Bronx
Black, Hugh D.....March
Bleich, Louis B.....Buffalo
Brodman, Harold R.....New York
Brummer, Donald L.....New York
Capraro, Vincent J.....Buffalo
Chassin, Norman.....Buffalo
Chessin, Herbert.....Far Rockaway
Ciepaitis, Victor J.....Brooklyn
Cooper, Norman S.....Riverdale
Delchamps, Harold J. Jr.....New York
Denman, Lewis G.....Livingston Manor
Dyckman, Jacob.....New York
Eberle, Richard D.....Syracuse
Fialkowski, Edward A.....Buffalo
Fleming, Thomas C.....New York
Forman, Robert L.....New York
Franklin, William D.....Kew Gardens
Friedman, David B.....New York
Fugitt, George W. Jr.....Buffalo
Goodstein, Seymour.....Brooklyn
Gordon, Hirsch L.....Bronx
Groff, Donald N.....Buffalo
Grover, Ralph W.....Bellerose
Hartman, John F. Jr...Hamburg, N. Y.
Hayden, Richard A.....Brooklyn
Hoffert, Paul W.....New York
Hoffman, Joseph.....Brooklyn
Hyman, George A.....New York
Jewett, Theodore C. Jr.....Buffalo
Leahey, Edward B.....Monroe
Long, John P.....Buffalo
McCarty, Frederick H.....Wellsville
Maclean, Donald W.....New York
Masterson, Joseph P.....Buffalo
Matlin, Melvin.....Brooklyn
Mazat, Alfred O.....New York
Nunez, Edgar O.....New York
O'Brien, John R.....Bronx
Osinski, Walter A.....Albany
Payne, James N.....Elmhurst
Rogers, William J. III.....Buffalo
Rutecki, Joseph E.....Buffalo
Schardt, Walter M.....Baldwin
Terry, Herbert S.....New York
Williford, Edward A. Jr.....New York

Tennessee

Bankston, Floyd N.....Knoxville
Black, Charles I.....Memphis
Cowan, Bennett Y.....Bristol
Doty, Robert D.....Rogersville
Hickman, James H.....Knoxville
Ogle, Homer C.....Sevierville
Smythe, Frank W. Jr.....Memphis
Taylor, Byron H. Jr.....Nashville
Whittle, Herbert P. Jr.....Knoxville

Utah

Brinton, Jay O.....Salt Lake City
Lubeck, Glenn H.....Ogden
Priday, Sidney M.....Smithfield
Southwick, Merlin P.....Salt Lake City
Taylor, Frederick R. Jr.....Provo

Vermont

Dimichele, John D.....Poultney
Muckley, Ralph W. Jr.....So. Woodstock

Virginia

Evans, Robert W. W.....Lynchburg
Gottschalk, Carl W.....Salem
Hough, Mac J.....Salem
Kelly, William E.....Charlottesville
Levy, David B.....Suffolk
Morris, John R. Jr.....Charlottesville
Morris, John S. Jr.....Lynchburg
Sager, William L.....Danville
Thornhill, Thomas M. Jr.....Lynchburg

West Virginia

Coury, John J. Jr.....Wheeling
Marvin, Samuel L.....Weirton
Sinnett, John F.....Superior
Squires, Russell D.....Fairmont

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

COLORADO

Committee to Review Newspaper Medical Advertising.—The Medical Society of the City and County of Denver, at the request for assistance from the advertising director of the *Denver Post*, has appointed a committee to review medical advertising for Denver papers. Members of the committee are Drs. Richard W. Whitehead, chairman, Roy L. Cleere, Maurice Katzman, Albert E. Evans and Herman S. Maul. The committee is to work in cooperation with the public policy committee of the medical society.

Expand Epilepsy Program.—Through a $5,000 annual grant from the Colorado Society for Crippled Children and Adults, the University of Colorado Medical Center, Denver, has expanded its epilepsy program. Dr. Harriot H. Hunter is director of the university's epilepsy clinic. The grant provides for a director, honorariums for two medical assistants, the services of a social worker, and for administrative services and supplies. Early projects include a registry of epileptics, an adult training program and a workshop to provide group therapy for parents as well as patients.

DELAWARE

State Medical Election.—At the annual September meeting of the Medical Society of Delaware, Dr. Mesrop A. Tarumianz, Farnhurst, was elected president for 1949; Drs. Gerald A. Beatty, Wilmington, secretary; Winfield W. Lattomus, Wilmington, treasurer, and James Beebe, Lewes, delegate to the American Medical Association, with Clyde C. Neese, Wilmington, as alternate.

ILLINOIS

Postgraduate Conference in Pekin.—The Illinois State Medical Society has arranged a conference for the Fifth Councilor District at the Pekin Country Club, Pekin, December 9. The speakers, all of Chicago, will be:

William T. Carlisle, Forewarning and Forearming in Obstetrics.
Chauncey C. Maher, Management of Cardiac Patients Pre- and Post-Operatively.
H. William Elghammer, Advances in Pediatrics.

At the dinner Dr. Percy E. Hopkins, Chicago, will discuss "Voluntary Prepayment Medical Care" and Dr. Chester C. Guy, Chicago, "Bleeding Peptic Ulcer."

Chicago

Lecture on Reconstruction of Face.—Sir Archibald McIndoe, chief of plastic surgery for the Royal Air Force during World War II, lectured on "Total Reconstruction of the Face Following Burns" at the University of Illinois College of Medicine November 10. Sir Archibald is senior plastic surgeon at St. Bartholomew's Hospital in London and surgeon at Queen Victoria Hospital in East Grinstead.

Dr. Lederer to Aid in Mexico's Hearing Program.—Dr. Francis L. Lederer, professor of otolaryngology and head of the department at the University of Illinois College of Medicine, has left for Mexico, where he will aid medical officials in formulating a national program for the hard of hearing. At the invitation of the Mexican undersecretary of health and welfare, he will travel through that country to conduct a survey of hearing and speech needs.

Survey of Cancer.—The Committee on Chicago-Cook County Health Survey reports that a questionnaire sent to doctors and hospitals in the city has indicated that more than 7,000 persons died of cancer and at least 15,000 new cases of cancer appeared in Chicago last year. The questionnaire was answered by 90 per cent of the physicians and 96 per cent of the hospitals queried. The next project will be to survey the problem of cancer in industry.

Dr. Lewy Receives Traditional Cane.—At the November meeting of the Chicago Laryngological and Otological Society Dr. Alfred Lewy was presented with the traditional cane of the society, which was started in circulation by the late Dr. Joseph C. Beck. It is held as the temporary property of the senior living member of the society and contains in its handle models of several otolaryngologic instruments. The late Dr. George E. Shambaugh was the preceding recipient of the cane.

Allergy Research Unit.—Northwestern University has established a research unit for allergy studies in the new allergy research laboratory under the general direction of Dr. Samuel Feinberg, chief of the division of allergy. Laboratory research is being directed by Dr. Saul Malkiel, newly appointed assistant professor of medicine at Northwestern. Initial support of the allergy research laboratory was implemented by grants from the U. S. Public Health Service and several pharmaceutical manufacturers.

Dr. Moruzzi at Northwestern University.—Dr. Giuseppe Moruzzi, Italian neurophysiologist, has been appointed to Northwestern University Medical School for a year of research by the Rockefeller Foundation, which last year established an annual visiting professorship in the university's Institute of Neurology. Dr. Moruzzi is director of the Institute of Human Physiology at the University of Parma, Italy, and professor of physiology in its medical school. He will devote most of his research to the physiology of the brain and the functional relation of the cerebellum to the cerebral cortex.

Five Illinois Professors Retire.—Five members of the faculty of the University of Illinois College of Medicine retired September 1, having reached retirement age: Dr. Selim W. McArthur, clinical professor of surgery; Dr. Clifford G. Grulee, Rush, clinical professor of pediatrics and former head of the department at Presbyterian Hospital; Dr. James H. Mitchell, Rush, clinical professor of dermatology and former head of the department of dermatology and syphilology at Presbyterian Hospital; Dr. Daniel B. Hayden, clinical professor of otolaryngology (Rush) and former head of the department at Presbyterian Hospital, and Dr. Morris Braude, clinical associate professor of psychiatry (Rush).

Certificates of Merit and Appreciation.—At a reception at the home of Chancellor Robert M. Hutchins of the University of Chicago, November 2, thirteen scientists of the university faculty were cited for their contributions to the war effort in presidential certificates of merit and of appreciation. Admiral Cary Jones, commandant, Ninth Naval District, and Lieutenant General Stephen J. Chamberlin, commanding general, Fifth Army, made the presentations. Among those receiving the certificate of appreciation were the following from the Toxicity Laboratory: Dr. Franklin B. McLean, first director of the Toxicity Laboratory; Dr. William B. Bloom, professor of anatomy; William L. Doyle, second director of the laboratory and associate professor of anatomy, and Dr. Eugene M. K. Geiling, chairman of the department of pharmacology. Among other faculty members receiving certificates of appreciation were William H. Taliaferro, Ph.D., chairman of the department of bacteriology and parasitology; Dr. E. S. Guzman Barron, associate professor of biochemistry, and Paul A. Weiss, professor of zoology. Among other Chicago scientists not on the faculty of the University of Chicago to be thus honored was Dr. Sidney O. Levinson, executive director of Michael Reese Research Foundation.

IOWA

Personal.—Dr. Hunter H. Comly was appointed assistant professor of pediatrics in the department of psychiatry at the State University of Iowa College of Medicine, Iowa City, effective September 1.

Dr. Rovenstine to Address Linn County Society.—At the December 16 meeting of the Linn County Medical Society in Cedar Rapids, Dr. Emery A. Rovenstine, New York, will speak on "Intravenous Use of Procaine and Its Derivatives." Drs. Stuart C. Cullen, Iowa City, and Florence D. Johnston, Cedar Rapids, will lead the discussion.

KANSAS

Refresher Course in Obstetrics and Gynecology.—A refresher course in obstetrics and gynecology will be presented December 6-8 at the University of Kansas Medical Center, Kansas City. Besides faculty of the University of Kansas, guest instructors will be Drs. John H. Moore, Grand Forks, N. D.; Lucien R. Pyle, Topeka; Lawrence M. Randall, Rochester, Minn., and Ray A. West, Wichita.

KENTUCKY

Hospital Advisory Board.—Dr. E. Bruce Underwood, Louisville, state health commissioner, has appointed five men as advisers on the administration of a state hospital plan. They are Dr. F. Guy Aud, Louisville, past president of the Kentucky State Medical Association; Dr. John W. Moore of the University of Louisville School of Medicine; Lee R. Curtis, Louisville, an

attorney; Dr. Joshua B. Lukins, Louisville physician, and Mr. S. A. Ruskjer, former president of the Kentucky Hospital Association. They will advise Dr. Underwood on the distribution of $500,000 this year and the same amount next year to Kentucky hospitals eligible for this state money.

LOUISIANA

Personal.—In honor of Dr. Urban Maes, New Orleans, at Touro Infirmary where he served for fifty years, a bronze plaque was recently unveiled. Charity Hospital also honored Dr. Maes in a like manner for forty-three years of service to that institution.

Dr. Lippard Goes to University of Virginia.—Dr. Vernon W. Lippard, dean since September 1946 of the Louisiana State University School of Medicine, New Orleans, has accepted the deanship of the University of Virginia Department of Medicine, Charlottesville, effective Feb. 1, 1949. Dr. Lippard is a graduate of Yale University School of Medicine, 1929. Before going to Louisiana he was associate dean of the Columbia College of Physicians and Surgeons, New York.

MINNESOTA

Residual Beneficiary of Doctor's Estate.—The University of Minnesota Medical School, Minneapolis, has been named a residual beneficiary of the $150,000 estate of the late Dr. James S. Reynolds of Minneapolis. The estate is to be placed in trust for Dr. Reynold's sister, on whose death the remainder of the estate is to be used as a scholarship fund in the medical school.

Establish Rehabilitation Center.—A rehabilitation center has been established at 279 Rice Street, St. Paul. A medical advisory board of seven doctors appointed by the Ramsey County Medical Society guides the medical policies of the center, the aims of which are prevention of unnecessary handicaps, restoration of function if possible, use of residual function and adjustment of patient to any residual disability. The three sponsoring agencies are the Minnesota Society for Crippled Children and Adults, Junior League of St. Paul, and the Wilder Charity.

NEW YORK

Food Service Training School.—A Food Service Training School has been opened at Hudson River State Hospital, Poughkeepsie, for instruction of institution employees and the development of high standards of food preparation and service in state institutions. The first class began October 11.

Eastman Memorial Lecture.—De René J. Dubos, Sc.D., a member of the Rockefeller Institute for Medical Research, New York, delivered the Eastman Memorial lecture on "Cellular Structures Concerned in the Pathogenesis of Tuberculosis" at the University of Rochester Medical School amphitheater November 19.

Mental Health Research Clinic at Buffalo.—The State Department of Mental Hygiene, in cooperation with the University of Buffalo School of Medicine, will set up a mental health research clinic in alcoholism at two leading Buffalo hospitals. The state department has made a grant to the clinic to implement in part a demonstration program.

Postgraduate Instruction.—The Medical Society of the State of New York with the cooperation of the New York State Department of Health has arranged the following postgraduate instruction programs: For the Oswego County Medical Society Dr. L. Maxwell Lockie, Buffalo, spoke on "Management of Arthritis" on November 16, 8:30 p. m., at the Elks Club, Fulton. On November 17 Dr. Locke L. Mackenzie, New York, addressed the members of the Fulton County Medical Society on "Use of Cell Smears in the Early Diagnosis of Cancer" at the Hotel Johnstown, Johnstown, 8:30 p. m.

New York City

Society News.—The Division of Mycology of the New York Academy of Sciences recently heard Norman F. Conant, Ph.D., Duke University School of Medicine, Durham, N. C., lecture on sporotrichosis. At the inaugural meeting October 22, officers elected were Drs. Frederick Reiss, president, and Royal M. Montgomery, secretary.

Harvey Lecture.—Dr. George K. Hirst, chief, Division of Infectious Diseases, Public Health Research Institute of the City of New York, delivered the second Harvey Lecture of the current series at the New York Academy of Medicine on November 18, on "The Biological Significance of the Virus Hemagglutinins."

Dr. Brown Named Acting Chairman of Medical Board.—Dr. Samuel A. Brown, formerly president of the New York Academy of Medicine and dean emeritus of the college of medicine, has been named acting chairman of the board of trustees of the New York University—Bellevue Medical Center, succeeding the late Richard W. Lawrence, LL.D. The board was formed in May to direct the affairs of the new medical center, which includes, in addition to the college of medicine, the Institute of Rehabilitation, the Institute of Industrial Medicine and the University Clinic. The medical center is also responsible through its teaching faculty for a major portion of the medical care given at Bellevue Hospital. Dr. Brown is a graduate of the University Medical College (New York University), 1894.

Dr. Senn Goes to Yale.—Dr. Milton J. E. Senn, professor of pediatric psychiatry and director of the Institute of Child Development at Cornell University Medical College, has been appointed Sterling professor of pediatrics and psychiatry and director of the new Yale University Child Study Center. The center, which will include the Yale Clinic of Child Development, will help parents, teachers and others concerned with problems of children. It will contain a guidance nursery, film library and clinical resources to supply research and teaching mediums for students interested in growth, development, behavior and personality. Dr. Senn received his M.D. degree from the University of Wisconsin Medical School, Madison, in 1927. He was an assistant professor of pediatrics at Cornell University Medical College in 1939, and then was made associate professor of pediatrics in psychiatry. Last year he was promoted to professor and was made director of the Institute of Child Development.

OHIO

Dr. Brailsford's Lecture.—At a special meeting of the Academy of Medicine of Cleveland Dr. James F. Brailsford, Birmingham, England, lectured on "Radiographic Evidence of Metastasis in Malignant Diseases" November 19 at the Medical Library Auditorium, 8:30 p. m. Dr. Brailsford is radiologist to the Queen Elizabeth's Hospital and the Royal Hospital for Crippled Children.

Professor Birkeland Named Department Head.—Jorgen M. Birkeland, Ph.D., professor of bacteriology of the Ohio State University College of Medicine, Columbus, and a member of the department staff since 1935, was recently made chairman of the department succeeding William A. Stark, Ph.D., who retired this year as emeritus professor of bacteriology (THE JOURNAL, April 10, page 994).

Sunday Afternoon Health Lectures.—A series of Sunday afternoon health lectures, free to the public, are being presented by the Academy of Medicine of Cleveland through its Health Education Foundation at the Medical Library Auditorium, 4 p. m.

Nov. 28, Harry V. Paryzek, Cleveland, Medical Emergencies; Farrell T. Gallagher, Lakewood, Surgical Emergencies.

Dec. 5, Elliott P. Joslin, Boston, Diabetes Yesterday, Today and Tomorrow.

Jan. 30, Roy W. Scott, Cleveland, Medical Aspects of Heart Disease; Claude S. Beck, Cleveland, Surgical Aspects of Heart Disease.

PENNSYLVANIA

Tribute to Dr. Donaldson.—In tribute to his thirty years' service as secretary to the Medical Society of the State of Pennsylvania, Dr. Walter F. Donaldson, Pittsburgh, was presented by members of the society with a combination television-radio-phonograph at the recent centennial celebration in Philadelphia. Dr. Donaldson accepted the gift from the stage of the Academy of Music, Philadelphia, before more than 3,000 physicians, their wives and invited guests.

Philadelphia

Dr. DeLamater to Direct Research.—The department of dermatology and syphilology of the University of Pennsylvania School of Medicine has announced the appointment of Dr. Edward D. DeLamater as associate research professor. He will act as director of research in the department and develop a mycology laboratory. Dr. DeLamater, a graduate of Columbia University College of Physicians and Surgeons, New York, 1942, has recently served on the staff of the Mayo Clinic, Rochester, Minn.

Pittsburgh

Symposium on Lung Cancer.—The meeting of the Allegheny County Medical Society on November 16 at 9 p. m. was devoted to a symposium on cancer of the lung. Subjects presented were "Diagnostic Value of Bronchial Secretions in Cancer of the Lung," "Present Day Concepts of Lung Cancer" and "Diagnosis and Modern Management of Cancer of the Lung."

SOUTH CAROLINA

Public Health Appointment.—Dr. William H. Chapman of Bishopville has been employed to serve with the Division of Maternal and Child Health of the State Board of Health. His work will be principally educational with emphasis on child growth and better family life. He will be available as speaker to local medical groups. Dr. Chapman graduated from the University of Maryland School of Medicine, Baltimore, 1929, and in recent years has served in the Richland-Columbia Venereal Clinic.

Society News.—The South Carolina Society of Ophthalmology and Otolaryngology, meeting at Charleston, elected Dr. Pierre G. Jenkins of Riverland Terrace as president and Dr. Roderick Macdonald of Rock Hill, secretary-treasurer.—— The North Carolina Eye, Ear, Nose and Throat Society elected Dr. James A. Harrill of Winston-Salem as president and Dr. MacLean B. Leath of High Point as secretary-treasurer. ——Dr. John R. Harvin of Sumter was recently elected president of the South Carolina Pediatric Society, and Dr. J. Rufus Bratton of Rock Hill, secretary-treasurer.

UTAH

Dr. Lawrence to Direct Cancer Teaching Program.—Dr. Edwin A. Lawrence has been named professor of surgery (oncology), and director of the cancer teaching program in the University of Utah College of Medicine, Salt Lake City. Dr. Lawrence was formerly director of the Tumor Clinic at Yale University and more recently has been in practice in thoracic surgery in Salt Lake City. He is a graduate of Western Reserve University School of Medicine, Cleveland, 1935, and served on the resident surgical staff at New Haven Hospital, Conn. In 1938 he was made a W. H. Cushing fellow in surgery at Yale University and was instructor in surgery there.

VIRGINIA

College to Award Ph.D. Degree.—The Medical College of Virginia, Richmond, will add to the list of degrees it may award that of Doctor of Philosophy in medical and related sciences. The college will limit its selection of candidates for the degree to a few highly qualified persons interested in pursuing work in medical and related sciences.

Personal.—Dr. William T. Sanger, president, Medical College of Virginia, Richmond, has been appointed a member of the National Advisory Committee for the social work education study sponsored by the National Council on Social Work Education. Dr. Ernest V. Hollis is director of the study, for which the Carnegie Corporation has made a grant of $31,000. The study began on October 1 and is expected to be concluded June 30, 1949.

WISCONSIN

Annual Dearholt Day.—The University of Wisconsin Medical School, Madison, in cooperation with the Wisconsin Anti-Tuberculosis Association, is presenting the ninth annual Dearholt Day program in the Service Memorial Institutes Building, Madison, 3 p. m. November 23. Dr. William S. Middleton, dean of the medical school, will act as chairman. Dr. Edith M. Lincoln, New York, will speak on tuberculosis and children. Florence B. Seibert, Sc.D., Philadelphia, will discuss the component parts of tubercle bacilli and their relation to the tuberculin test. The program will be presented in Milwaukee both by the Marquette University School of Medicine and the Milwaukee County Medical Society on the preceding day and it will also service as a monthly meeting of the Dane County Medical Society at the Madison Club on Tuesday evening. Dr. Dearholt was executive secretary of the Wisconsin Anti-Tuberculosis Association from 1908 until his death in 1939.

WYOMING

State Medical Election.—The Wyoming State Medical Society installed Dr. George E. Baker, Casper, as president, and chose Dr. Dewitt Dominick, Cody, president elect; Dr. Peter M. Schunk, Sheridan, as treasurer, and Dr. Roscoe H. Reeve, Casper, delegate to the American Medical Association, with Dr. William A. Bunten, Cheyenne, as alternate.

ALASKA

Crippled Children's Headquarters.—The new $50,000 headquarters building of the Alaska Association of the International Society for Crippled Children was dedicated September 7 in Anchorage. Governor Ernest H. Gruening, Dr. Philip H. Moore, Mount Edgecumbe, orthopedic surgeon, Dr. C. Earl Albrecht, Juneau, territorial commissioner of health, and Dr. Catherine S. Sherwood, Juneau, director of the Crippled Children's Service of Alaska, took part. The center was completed this fall after three years of planning and fund raising to support the orthopedic hospital and the headquarters.

GENERAL

New Editor of Journal of Immunology.—Dr. Arthur F. Coca, Pearl River, N. Y., has resigned as editor of the *Journal of Immunology*, a position he had held since the foundation of the journal in 1916, and will now serve as associate editor. His successor is Dr. Geoffrey Edsall, Boston, director of the Antitoxin and Vaccine Laboratory of the State of Massachusetts.

Medical Mission to Colombia.—The Unitarian Service Committee has announced a medical mission to Colombia to be staffed by Drs. George H. Humphreys, New York, chairman; McKeen Cattell, New York; Rafael Domingues, Cleveland; Carney Landis, Ph.D., New York; Dr. Salvatore P. Lucia, San Francisco; Dr. Donovan J. McCune, New York, and Dr. Perry P. Volpitto, Augusta, Ga. Lectures will be given by the team on surgery, pharmacology, pathology, internal medicine, pediatrics, anesthesiology and psychology.

Southern Surgical Association.—The annual session of the Southern Surgical Association will be held at the Greenbrier Hotel, White Sulphur Springs, W. Va., December 7-9, under the presidency of Dr. Edwin P. Lehman, Charlottesville, Va. Among the subjects of papers to be presented are hyperthyroidism in children, surgical treatment of lesions of the suprarenal gland, partial hepatectomy with intrahepatic cholangiojejunostomy, amebic hepatic abscesses—prevention and treatment, and status of the surgical treatment of hypertension. The association dinner will be Wednesday evening at 7 o'clock, when Dr. Lehman will give the president's address.

Conference on Rehabilitation.—Community Organization for Rehabilitation will be the theme of the National Rehabilitation Association Conference at the Hotel Loraine, Madison, Wis., December 6-10. The program includes panel discussions on In What General Areas the Public and Voluntary Rehabilitation Agencies May Cooperate, Community Organization to Secure Adequate Legislation, Community Organization in Development and Use of Medical Rehabilitation Facilities and Community Organization for Public Relations. Requests for hotel reservations should be addressed to A. E. Towne, Rehabilitation Division, 320 State Office Building, Madison 2.

Society Elections.—The Southern Medical Association installed Dr. Oscar B. Hunter, Washington, D. C., as president, and chose Dr. Hamilton W. McKay of Charlotte, N. C., as president-elect at its recent convention in Miami, Florida. Cincinnati was selected as the convention city for 1949.——At the recent annual meeting of the American Society of Clinical Pathologists in Chicago October 12 to 15, Dr. Osborne A. Brines, Detroit, was installed as president, and Dr. James B. McNaught, Denver, was chosen president-elect. On the resignation of Dr. Alfred S. Giordano, South Bend, as secretary-treasurer, Dr. Clyde G. Culbertson, Indianapolis, was appointed to fill the unexpired term.

Van Meter Prize Award.—The American Goiter Association again offers the Van Meter Prize Award of $300 for the best essay on problems related to the thyroid gland. The award will be made at the annual meeting of the association in Madison, Wis., May 26-28, 1949, providing that essays of sufficient merit are presented. The competing essays should not exceed three thousand words and must be presented in English; a typewritten double-spaced copy must be sent to the Corresponding Secretary, Dr. Thomas C. Davison, 207 Doctors Building, Atlanta 3, Ga., not later than March 15, 1949. A place will be reserved on the program for presentation of the prize award essay by the author if it is possible for him to attend. The essay will be published in the annual proceedings of the association. This will not necessarily prevent its further publication in any journal selected by the author.

WHO Regional Organization.—The first World Health Organization's regional group was established at the conference of the South East Asia Regional Committee of the organization October 4 at New Delhi, India. It is the first such body among five or six to be set up in major geographic areas throughout the world as soon as the majority of countries in each area agree to participate. The regional organizations were authorized by the World Health Assembly last summer. Delegates from India, Siam, Ceylon, Burma and Afghanistan, together with observers from Nepal and French India as well as from the United Nations and its specialized agencies agreed on structure and program of the regional group. The World Health Organization's Executive Board will be requested to authorize by January 1 the establishment of the South East Asia Regional Office with Delhi proposed as its site.

Poliomyelitis Continues Epidemic in Some Areas.—According to the U. S. Public Health Service, the incidence of poliomyelitis continues above normal in a few areas although the decline is following the seasonal picture. A total of 830 cases was reported for the week ended November 4 as compared with

1,079 for the preceding week, 715 for the corresponding week in 1946, and a five year median of 489 for the week. Reported incidence declined in California from 206 to 198, in South Dakota from 121 to 58, in North Carolina from 42 to 29, in Ohio from 52 to 14, in Illinois from 41 to 21, in Wisconsin from 47 to 32 and in Iowa from 79 to 44. Incidence increased in Michigan from 39 to 52 and in Texas from 28 to 31. A total of 23,074 cases had been reported up to November 4, as compared with 22,377 in 1946, 9,195 in 1947 and a five year median of 11,952 for the corresponding period.

Ella Sachs Plotz Foundation.—The annual report of the Ellis Sachs Plotz Foundation for the Advancement of Scientific Investigation lists fifteen grants made during the current year to research workers in the United States, Europe and Asia. Grants are given in sciences related to medicine and usually will not exceed $500 but may be up to $1,000. Applications for the year 1949-1950 must be in the hands of the executive committee before April 15. Letters asking for aid must state definitely qualifications of the investigator and an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. Applicants should state whether or not other foundations have been approached for financial assistance and what other sources of support are relied on for research. Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston 14.

Dr. Armstrong Given Prentiss Award.—Dr. Donald B. Armstrong, New York, received the fifth Elisabeth S. Prentiss National Award in Health Education at the luncheon meeting of the American Public Health Association, Boston, November 9. Selection of Dr. Armstrong was based on his 1916 survey and study which led to the establishment of the Framingham, Mass., community health and tuberculosis experiment; his survey in 1920 that resulted in the first national health council, which he headed for several years; his work as secretary to the Milbank Memorial Fund Technical Board and his work as second vice president of the Metropolitan Life Insurance Company, New York, where he has been in charge of the health and welfare service for policy holders. The Prentiss Award was established in 1943 by the Cleveland (Ohio) Health Museum for encouragement of more and better work in the field of health education and is named in honor of the memory of the museum's first foundation benefactor, who also gave it its first home.

International Congress on Rheumatic Diseases.—The seventh International Congress on Rheumatic Diseases will be held at the Hotel Waldorf-Astoria, New York, May 30-June 3, 1949, under the sponsorship of the International League Against Rheumatism. The U. S. State Department will cooperate in issuing official invitations to various governments and rheumatism associations. Invited guests will be the members of the International League, the European League and Pan American League against Rheumatism with their constituent organizations. It is estimated that the program will include 80 to 100 papers, 70 invited discussants, 5 topics for panel discussions by about 30 participants and 15 clinics. Those who contemplate the presentation of papers should submit titles to the program committee for consideration before Jan. 1, 1949. Information may be obtained by writing Dr. Ralph Pemberton, 1901 Walnut St., Philadelphia, president of the International League, or Dr. J. Van Breemen, Keizersgracht 489 Amsterdam, Netherlands, secretary general.

Dr. Muller Delivers Sigma Xi Lectures.—Herman J. Muller, D.Sc., 1946 Nobel prize winner and professor of zoology at Indiana University, Bloomington, will present the results of his investigations on roentgen treatment of certain diseases in connection with the Sigma Xi Lectureship at colleges and universities in November, December and January. The lecture will be presented at the following institutions:

Nov. 15, Joint lecture to be held at Pullman, Wash., for the State College of Washington, Pullman, and the University of Idaho, Moscow.
Nov. 17, University of Washington, Seattle.
Nov. 19, Oregon State College, Corvallis.
Nov. 22, University of Oregon, Eugene.
Nov. 29, Stanford University, Palo Alto, Calif.
Dec. 1, University of California, Davis.
Dec. 3, University of Nevada, Reno.
Dec. 6, University of California, Berkeley.
Dec. 8, University of Utah, Salt Lake City.
Dec. 9, Brigham Young University, Provo, Utah.
Dec. 10, Utah State Agriculture College, Logan.
Dec. 13, Colorado A. and M. College, Fort Collins.
Dec. 15, Illinois Institute of Technology, Chicago.

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Jan. 18, The Abbott Research Laboratories, North Chicago, Ill.
Jan. 20, University of Wisconsin, Madison.
Jan. 21, Northwestern University, Evanston, Ill.

FOREIGN

Fund for Research on Rheumatism.—The Nuffield Foundation, a philanthropic organization in England, has received $1,800,000 from Captain Oliver Bird, wealthy Birmingham manufacturer, to promote research in the prevention and cure of rheumatism, according to the *Chicago Daily News*.

Textbooks on Nursing for Japan.—The American Red Cross, through the efforts of Edith Olson, Red Cross nursing consultant now in Tokyo, has given the Japanese Red Cross 130,000 pounds of paper stock which will be used to publish textbooks on home nursing, midwifery, nursing administration, public health and a reprinting of the "Nursing Procedure Manual." A portion of the paper has already arrived in Japan and production of the textbooks has begun.

Congress of Obstetrics and Gynecology.—The British Congress of Obstetrics and Gynaecology will be held in the Friends' Meeting House, Euston Road, London, July 1949. Papers will be presented by Dr. Joe V. Meigs, Boston, Mass.; Dr. Charles McIntosh Marshall, Liverpool; Dr. Gerald I. M. Swyer, London; Dr. Francis J. Browne, London, and Dr. Derrick M. Dunlop, Edinburgh. Owing to present difficulties in arranging hotel accommodations and travel, secretaries would like to have, by March 31, 1949 at the latest, the names of those who hope to attend.

Antituberculosis Drive in India.—The first nationwide BCG vaccination campaign in India, designed to lower the rate of tuberculosis among children and adolescents, was inaugurated in September at Madanapalle, near Madras. The program will be carried out jointly by the Indian health authorities and the World Health Organization, which last May sent a team of experts on tuberculosis to India at the government's request. Since transportation of BCG vaccine from Europe was unreliable, the World Health Organization also sent a pharmacologist to India to assist in setting up a laboratory which is now producing the vaccine. The number of tuberculosis cases in India is estimated at 2,500,000 annually out of a total population of 320,000,000, and the disease causes more than 500,000 deaths each year. The Indian program is part of the global antituberculosis campaign which the World Health Organization designated for priority action in 1949.

Marriages

ROYAL GREEN JENNINGS JR., Thomasville, N. C., to Miss Treva Bullard Miller of Winston-Salem, October 2.

WILLIAM RALPH DEATON JR.,, Greensboro, N. C., to Miss Frances Kirksey of San Antonio, Texas, recently.

MICHAEL JOSEPH COFFEY, Belmar, N. J., to Miss Mary Jane Maas of Neptune at Asbury Park, September 18.

CHARLES M. PARKER, Kelford, N. C., to Miss Anne A. Westphal at Fredericksburg, Va., September 4.

WILLIAM THOMAS ELLIS, Schenectady, N. Y., to Miss Edna Margaret Murphy of Hamden, Conn., June 12.

S. MICHAEL ERBA, New Haven, Conn., to Miss Marcella La Reau Kytchen of Roanoke, Va., July 31.

ROBERT LEWIS NELSON, New Berlin, N. Y., to Miss Catherine Rosemary Bertelli of Woodhaven, recently.

ADA ELEANOR BIFFAR, Whitestone, N. Y., to Mr. Edward A. Ryan of Forest Hills, N. Y., recently.

DONALD H. GLEW JR., to Mrs. Patricia Cummings Garrity, both of Washington, D. C., October 2.

THOMAS MANLEY FLANAGAN to Miss Esther Ann Coyne, both of Norwich, N. Y., September 11.

JOHN THOMPSON PRIOR, Syracuse, N. Y., to Mrs. Elizabeth Titus Troy of Binghamton, July 24.

DANIEL H. CANNON, New Albany, Ind., to Miss Marilynn E. Carr of Delanco, N. J., October 2.

WILLIAM H. SCHLITZER, to Miss Helen Horan, both of Pottsville, Pa., in Philadelphia, July 17.

ANTONI MILLS DIEHL to Miss Sybil Reid Bothwell, both of Newburyport, Mass., September 7.

IRA DEYO LE FEVRE JR., to Miss Helen Tate Rhodes, both of Schenectady, N. Y., July 24.

JAMES N. DEWANE to Miss Patricia Mullins, both of Menominee, Mich., September 11.

WILLIAM E. HIGGS to Mrs. Rae Myers, both of Cuba, N. Y., September 4.

Deaths

Abraham Myerson ✠ Boston; born in Yanova, Russia, Nov. 23, 1881; Tufts College Medical School, Boston, 1908; served as clinical professor of psychiatry at the Harvard Medical School and the graduate school; professor of neurology emeritus at his alma mater; at one time on the faculty of St. Louis University School of Medicine; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member and formerly second vice president of the American Neurological Association; member of the American Psychiatric Association and the New England Society of Psychiatry; member and past president of the American Psychopathological Society; member of the Commission on Research in Mental Health, Commonweath of Massachusetts; served on the staffs of the McLean Hospital in Belmont and the Boston State, Beth Israel, Boston City, Boston Psychopathic, and Washingtonian hospitals; pathologist and clinical director of the State Hospital in Taunton, Mass., from 1914 to 1918; member of the Jewish Academy of Arts and Sciences; author of "Foundations of Personality," "Inheritance of Mental Diseases," "When Life Loses Its Zest" and other books; died September 3, aged 66, of cardiac decompensation.

William Payne Thompson, Princeton, N. J.; Columbia University College of Physicians and Surgeons, New York, 1924; formerly on the faculty of his alma mater; fellow of the American College of Physicians; member of the American Society for Clinical Investigation; president of the board of managers of the New Jersey State Hospital, Marlboro, and consultant at the Fitkin Memorial Hospital in Asbury Park; for many years on the staff of the Presbyterian Hospital; on the staff of the Mercer Hospital in Trenton; member of the board of trustees of the Trudeau (N. Y.) Sanatorium; died in the New York Hospital August 10, aged 50.

Edgar Ephraim Shifferstine ✠ Tamaqua, Pa.; born Oct. 1, 1874; University of Pennsylvania Department of Medicine, Philadelphia, 1899; fellow of the American College of Surgeons; member of the American College of Hospital Administrators; director of clinics for rheumatic heart disease, state department of health; at one time surgeon in the U. S. Public Health Service reserve with the rank of major; president of the school board; served on the staffs of the Coaldale (Pa.) State Hospital and the Pottsville (Pa.) Hospital; director of the Tamaqua National Bank; died in the Abington (Pa.) Memorial Hospital August 22, aged 73, of carcinoma of the pancreas.

Charles Randolph Keith Swetnam ✠ Prescott, Ariz.; born in Falmouth, Va., in 1882; Georgetown University School of Medicine, Washington, D. C., 1904; specialist certified by the American Board of Otolaryngology; past president of the Arizona State Medical Association and of the Yavapai County Medical Society; fellow of the American College of Surgeons; member of the American Academy of Ophthalmology and Oto-Laryngology and of the Pacific Coast Oto-Ophthalmological Society; a member and past president of the Prescott Community Hospital staff; died August 6, aged 66, of carcinoma of the prostate.

Wallace E. Belt, Dodge Center, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1889; died July 18, aged 91.

Harry Boyd-Snee, Los Angeles; Rush Medical College, Chicago, 1889; fellow of the American College of Surgeons; formerly practiced in South Bend, Ind., where he was on the staff of St. Joseph's Hospital; served during World War I; major, medical reserve corps not on active duty; died July 5, aged 79, of terminal bronchopneumonia.

Isham Lester Cummings ✠ Ada, Okla.; Chicago College of Medicine and Surgery, 1912; on the staff of Valley View Hospital; died July 23, aged 58, of coronary occlusion.

Frank Daniel Elkavich ✠ Troy, N. H.; McGill University Faculty of Medicine, Montreal, Canada, 1937; past president of the Cheshire County Medical Society; served during World War II; on the staffs of Quincy City (Mass.) Hospital and the Elliot Community Hospital in Keene, where he died July 27, aged 39, of injuries received in an automobile accident.

Isabella Maud Garnett, Evanston, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; formerly superintendent of Community Hospital, where she died August 23, aged 76, of uremia, hypertension and heart disease.

Arthur R. Hansen ✠ Chicago; Chicago College of Medicine and Surgery, 1913; served during World War I; on the staff of the Henrotin Hospital, where he died September 11, aged 60, of hypostatic pneumonia following injuries received in a fall.

Charles Russel Hartsook ✠ Wichita Falls, Texas; Medical College of Virginia, Richmond, 1904; fellow of the American College of Surgeons; specialist certified by the American Board of Otolaryngology; past president of the Wichita County Medical Society; formerly councilor of the Third District of the State Medical Association of Texas; organizer of the Texas Society of Ophthalmology and Otolaryngology; affiliated with the Wichita General Hospital; died July 14, aged 74, of septicemia and myocarditis.

Euel Park Hathaway, Lawton, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1929; director of the city-county health department; died July 13, aged 45, of cirrhosis of the liver.

Frederick Henry Hollingsworth, Okmulgee, Okla.; Kansas City (Mo.) Medical College, 1901; formerly county clerk; died in Oklahoma City July 17, aged 74, of heart disease.

Theodore Holtan ✠ Waterville, Minn.; Milwaukee Medical College, 1911; died August 22, aged 65, of heart disease.

Henry Pope Howard, Everett, Wash.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; member of the American Medical Association; fellow of the American College of Surgeons; died July 24, aged 81, of lobar pneumonia.

Charles Franklin Junkermann, Columbus, Ohio; the Hahnemann Medical College and Hospital, Chicago, 1889; died August 29, aged 86, of arteriosclerosis.

William Wolf Kahn, Van Nuys, Calif.; Baltimore University School of Medicine, 1896; died August 31, aged 81.

William Joseph Kennedy ✠ Newark, Ohio; Georgetown University School of Medicine, Washington, D. C., 1905; on the staff of the Newark City Hospital; died July 16, aged 69, of carcinoma of the bladder.

Olin Arvin Kimble ✠ Murdo, S. D.; Rush Medical College, Chicago, 1908; member of the local draft board during World War I; for many years city councilman; vice president of the Jones County Bank; died August 24, aged 70, of leiomyosarcoma.

Henry Eugene King ✠ Fullerton, Neb.; John A. Creighton Medical College, Omaha, 1903; past president and secretary of the Nance County Medical Society; served during World War I; city physician; died in the Veterans Administration Hospital, Lincoln, August 25, aged 72, of heart disease.

Sterling Covert King, Watsontown, Pa.; Temple University School of Medicine, Philadelphia, 1922; member of the American Medical Association; served during World War I; affiliated with the Williamsport (Pa.) Hospital; died September 16, aged 52, of heart disease.

Edward Larkin ✠ Washington, D. C.; Georgetown University School of Medicine, Washington, 1908; professor of clinical orthopedic surgery at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; served overseas during World War I; affiliated with the Veterans Administration Hospital in Mount Alto, and the Georgetown University Hospital, where he died August 18, aged 66, of arteriosclerosis.

Marshall Aiken Leach ✠ Canonsburg, Pa.; Northwestern University Medical School, Chicago, 1940; president of the Canonsburg Borough Council; certified by the National Board of Medical Examiners; affiliated with Canonsburg General Hospital and the Pennsylvania Training School at Morganza; died in St. Francis Hospital, Pittsburgh, August 26, aged 36.

Eli Long, Cresco, Pa.; Columbia University College of Physicians and Surgeons, New York, 1896; member of the American Medical Association and the Medical Society of the State of New York; at one time on the faculty of the New York Post Graduate Medical School and Hospital, Columbia University; served during World War I; served on the staffs of Willard Parker and Presbyterian hospitals in New York; formerly medical director of the Bankers Trust Company; died August 3, aged 77, of coronary embolism.

George E. MacKinnon, Prentice, Wis.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1914; member of the American Medical Association; died in the Sacred Heart Hospital, Tomahawk, August 17, aged 61.

Edward Emmett McMahon, Omaha; John A. Creighton Medical College, Omaha, 1920; served as assistant professor of medicine at his alma mater; formerly medical director of Douglas County Hospital and on the staffs of Methodist, St. Joseph's, St. Catherine's and Immanuel hospitals; formerly affiliated with Veterans Administration Hospital in West Los Angeles; died August 19, aged 56, of coronary disease.

Edward Martin Miers, Mena, Ark.; University Medical College of Kansas City, 1910; member of the American Medical Association and the International College of Surgeons; president of the Polk County Medical Society; formerly on the staff of the Wesley Hospital in Kansas City, Mo.; died July 9, aged 62.

Isaac Julius Martinson, New York; University of Dorpat Faculty of Medicine, Russia, 1897; member of the American Medical Association; died August 24, aged 75, of coronary thrombosis.

Charles Carl Montano, Hartford, Conn.; Tufts College Medical School, Boston, 1935; member of the American Medical Association; served in the U. S. Public Health Service reserve attached to the Coast Guard from April 1943 to April 1946; affiliated with St. Francis and Hartford hospitals; died July 14, aged 38, of coronary thrombosis.

Oscar Nagel, Detroit; University of Michigan Medical School, Ann Arbor, 1932; member of the American Medical Association; served in the medical corps, Army of the United States, during World War II; died August 22, aged 48, of coronary heart disease.

Isaac DeWayne Nelson, River Rouge, Mich.; Meharry Medical College, Nashville, Tenn., 1945; interned at the Harlem Hospital in New York; certified by the National Board of Medical Examiners; on the staff of the Sidney A. Sumby Hospital; drowned while swimming near Amherstburg, Ontario, August 15, aged 29.

James Nisles Nesbitt, Gaffney, S. C.; University of Tennessee Medical Department, Nashville, 1889; member of the American Medical Association; died August 29, aged 81, of carcinoma of the colon.

Rea Parker ✠ Smithfield, Va.; University College of Medicine, Richmond, 1908; also a graduate in pharmacy; past president and secretary of the Isle of Wight County Medical Society; county coroner and chairman of the county school board; active in Boy Scout work and in 1945 received the Silver Beaver; died August 2, aged 67, of coronary thrombosis.

Andrew B. Parr, Gonzales, Texas; Keokuk (Ia.) Medical College, 1892; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1905; died in Petaluma, Calif., August 10, aged 78.

Helen Myrtle Patton, Chicago; Northwestern University Medical School, Chicago, 1944; member of the American Medical Association; clinical assistant in the department of medicine at her alma mater; medical administrative assistant to the superintendent and a member of the hospital staff of Wesley Memorial Hospital, where she died August 4, aged 50.

John Birdsall Paul ✠ Kansas City, Mo.; Kansas City (Mo.) Medical College, 1897; affiliated with the Research Hospital, where he died August 14, aged 77, of carcinoma with metastases.

Vincent Sylvester Pawelek Jr., ✠ Houston, Texas; Baylor University College of Medicine, Dallas, 1943; interned at the Robert B. Green Memorial Hospital in San Antonio; served during World War II; killed instantly August 6, aged 29, in an automobile accident near Eunice, La.

Roy Gates Perham, Hasbrouck Heights, N. J.; Syracuse University College of Medicine, 1912; member of the American Medical Association; health officer and school physician for many years; on the staff of Hackensack (N. J.) Hospital; died August 4, aged 60, of cerebral hemorrhage.

Charles Pines, New York; University and Bellevue Hospital Medical College, New York, 1911; assistant clinical professor of dermatology and syphilology at his alma mater; on the staff of Bellevue Hospital; died in Mount Sinai Hospital August 21, aged 64, of coronary occlusion.

Mastin Lee Pipes, Moreland, Ky.; Hospital College of Medicine, Louisville, 1894; member of the American Medical Association; died August 14, aged 75, of injuries received when the automobile in which he was driving was struck by a train.

Lee Roy Plaugher ✠ Denver; University of Colorado School of Medicine, Denver, 1927; served in France during World War I; affiliated with Porter Sanitarium and Hospital and St. Anthony Hospital, where he died August 10, aged 53, of arteriosclerotic heart disease.

Irvin Immanuel Pogue, Scott, Miss.; University of Tennessee College of Medicine, Memphis, 1916; member of the American Medical Association; died August 26, aged 57, of leukemia.

Clark Crandall Post, Barron, Wis.; College of Physicians and Surgeons of Chicago, 1893; served during World War I; died August 4, aged 81, of cerebral hemorrhage.

William Porter Pratt, Quincy, Mass.; Tufts College Medical School, Boston, 1907; member of the American Medical Association; on the staff of the Quincy City Hospital; died August 15, aged 71.

Alfred Pulford, Toledo, Ohio; Homeopathic Hospital College, Cleveland, 1885; died August 4, aged 85, of cerebral thrombosis.

Israel Kay Redd, Ellerson, Va.; Medical College of Virginia, Richmond, 1914; member of the American Medical Association; died in St. Luke's Hospital, Richmond, August 21, aged 55, of coronary artery disease.

Frances A. Ring, Chicago; Harvey Medical College, Chicago, 1903; member of the American Medical Association; served as examining physician at the Juvenile Court; died August 20, aged 86, of Buerger's disease and gangrene of the right foot.

Budd Robbins ✠ Hanford, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; died August 17, aged 61.

Hector Morrison Ross, Chicago; University of Illinois College of Medicine, Chicago, 1926; member of the American Medical Association; affiliated with the Martha Washington Hospital; died August 27, aged 47, of coronary occlusion.

Hollace Rector Royster ✠ Frankfort, Ind.; University of Illinois College of Medicine, Chicago, 1917; died August 6, aged 59.

Raymond Wentworth Runyan ✠ Panama, Republic of Panama; Medical College of Ohio, Cincinnati, 1905; member of the Medical Association of the Isthmian Canal Zone; fellow of the American College of Surgeons; on the staff of the Hospital de Panama; died September 17, aged 63, of heart disease.

William Carl Schmidt ✠ Augusta, Mo.; St. Louis College of Physicians and Surgeons, 1898; died in St. Joseph Hospital, St. Charles, August 9, aged 74.

Lester L. Scott, Siloam Springs, Ark.; University of Louisville (Ky.) Medical Department, 1907; member of the American Medical Association; died August 11, aged 65.

Levi Tillman Slayden, Tuckerman, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1894; Missouri Medical College, St. Louis, 1895; died August 23, aged 73.

Edward Byrnes Smith, Shelbyville, Ky.; Chicago Homeopathic Medical College, 1895; died August 5, aged 76, of angina pectoris.

James Walker Smith, Miami, Fla.; Northwestern University Medical School, Chicago, 1894; member of the American Medical Association; fellow of the American College of Surgeons; at one time practiced in Baguio and Manila in the Philippine Islands; died in Jackson Memorial Hospital August 14, aged 78, of bronchopneumonia.

Peder Soe ✠ Kimballton, Iowa; Chicago Homeopathic Medical College, 1893; past president of the Audubon County Medical Society; served on the school board and town council; bank president; died in a hospital at Council Bluffs August 18, aged 86, of heart disease.

Alvin P. Stauffer, Hagerstown, Md.; Pulte Medical College, Homeopathic, Cincinnati, 1885; member of the American Medical Association; formerly member of the county board of education; died August 3, aged 91, of senility.

Thomas Turner Thomas ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1895; formerly on the faculty of his alma mater and of the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; fellow of the American College of Surgeons; an Affiliate Fellow of the American Medical Association; affiliated with Northeastern Hospital; died in Avon, N. J., August 7, aged 82, of arteriosclerosis.

James Handy Truitt, Glenn Dale, Md.; Chattanooga (Tenn.) Medical College, 1904; also a graduate in pharmacy; served during World War I; past president of the Prince Georges County Firemen's Association; formerly on the staff of the Casualty Hospital; died in the Mount Alto Hospital, Washington, D. C., August 8, aged 78, of heart disease.

Abraham Wallerstein, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1924; member of the American Medical Association; on the staff of the Beth Moses Hospital; died in Doctors Hospital August 8, aged 48, of carcinoma of the liver.

Wallace W. Wheat, Rosedale, Ind.; Eclectic Medical Institute, Cincinnati, 1899; died recently, aged 70.

Boyd Thompson Williams, Hudson, Wis.; Cincinnati College of Medicine and Surgery, 1901; died August 9, aged 71, of myocardial degeneration and purpura hemorrhagica.

Foreign Letters

PARIS

(From Our Regular Correspondent)

Oct. 14, 1948.

First Human Case of "Black Disease of Sheep"

Mollaret and Guéniot have just reported to the Société Médicale des Hôpitaux de Paris observation of severe icterus in yellow atrophy of the liver due to an anerobic microbe, Clostridium oedematiens (Weinberg and Séguin 1915). A patient with general paralysis with positive Wassermann reaction (3 plus) in the blood and the special fluid was, after twenty-one days of observation, transferred in a generally good state to the ward of the authors for therapeutic malaria. Suddenly, the next day, he was seriously ill with a temperature of 39.5 C. (102.2 F.), subicterus at the level of the conjunctivas without hemorrhagic syndrome and a feeble pulse with a rate of 126. Abdominal examination did not reveal abnormality, but the dulness of the liver could hardly be outlined and there was oliguria with neither albuminuria nor glycosuria. The state of the patient became worse from hour to hour; the icterus increased in the afternoon, and the patient fell into a deep coma. He died during the night. Autopsy revealed the presence of Cl. oedematiens in a pure state, necrosis of hepatic cells, but the conservation of the architecture of the lobule and integrity of the vessels and of the bile duct. The kidneys presented necrosis of the epithelial cells. The good state of the pancreas and of the spleen and the conservation of the spermatozoa in the testicles prove that the aforementioned injuries were not due to the cadaveric autolysis, but to the toxin of the Cl. oedematiens. Hitherto this anerobe was only known as a cause of the peracute degenerative necrosing hepatitis of sheep, "the black disease." This first human case is worth being reported, as it adds a new causation for peracute severe primitive icterus. The authors emphasize that an immediate treatment with massive doses of specific antitoxin and penicillin might be effective in other possible cases.

Exchange Transfusions in Acute Leukemia

In the Paris letter of March 30, 1948, published in THE JOURNAL May 22, page 400, treatment of acute leukemia by means of exchange transfusions by Drs. Bessis and Bernard was reported. P. Croizat Révol and his collaborators reported to la Société Médicale des Hôpitaux de Lyon 5 cases of acute leukemia treated by the same method.

By repeated exchange transfusions (15 to 20 liters of injected blood), the authors obtained a noticeable lowering of the number of white blood cells, an increase in the number of red cells and a remarkable improvement in the medullary and blood formula in several cases, but this effect was only temporary (it lasted three months in 1 case). The patients died later, in spite of the repetition of the same treatment, combined sometimes with cautious radiotherapy.

Exchange Transfusions in Acute Azotemic Nephritis

Professor Pasteur-Valery-Radot, P. Milliez and their collaborators have just reported observation of a case of acute post abortum nephritis following septicemia due to Clostridium welchii.

Twenty-four hours after the beginning of this disease, one noted generalized icterus, extreme oliguria with hemoglobinuria, azotemia (2 Gm.) and anemia (1,600,000 red blood cells). Under the influence of penicillin therapy, immediately instituted, the septicemia disappeared. The second day of the disease, an exchange transfusion of 7 liters was made; this removed the effects of the icterus and did away with the anemia in a few hours, but the azotemic nephritis persisted. During sixteen days of oliguria, when the blood urea reached 4 Gm. per liter, the authors gave four exchange transfusions (totaling 21.35 liters). Suddenly, on the seventeenth day, diuresis was established without modification of the urea concentration of the urine, which stayed at 6 to 8 Gm. per thousand. The blood urea fell progressively to reach a normal rate on the twenty-fifth day. The author made a sixth exchange transfusion twenty-four hours after the reestablishment of diuresis. This treatment prevented the azotemia from increasing in spite of the extreme oliguria and permitted awaiting for restoration of diuresis. The authors insist on the harmlessness and ease of this method and on its advantages over peritoneal dialysis, intestinal perfusion and the artificial kidney, application of which is more difficult.

A. Tzank and J. Dausset have also used this treatment in 3 cases of anuria. In a case of scarlatinal nephritis with anuria, with blood urea at 3.25 Gm. per thousand, pulmonary edema and fall of arterial tension, an exchange transfusion gave a spectacular result: Diuresis was reestablished suddenly (3 liters) with a urea concentration at 15.11 Gm. per liter. Recovery was rapid and complete. Complete urinary tests showed that the renal balance was normal.

In a case of mercurial nephritis with extreme oliguria, the first exchange transfusion of 4.5 liters immediately improved the general state; next day diuresis was established. The urea concentration in the urine varied from 10.3 to 14.95 Gm., but the effect rapidly diminished in spite of repeated exchange transfusions (unfortunately in insufficient quantity). The patient died on the twenty-fifth day of her illness with toxic myocarditis. The amount of urine in twenty-four hours had reached 760.3 cc.; the blood urea was 5.5 Gm. per liter, and the urea in the urine 8.45 Gm. The autopsy showed big pale kidneys, without renal sclerosis, with lesions which were probably not irreversible.

In another case of mercurial nephritis with anuria, the authors gave eight exchange transfusions totaling 29.25 liters of blood, diluted one third. Diuresis was reestablished, blood urea was progressively reduced from 3.5 to 0.95 per liter, and urea concentration in the urine was increased.

The authors emphasize that the carrying out of the treatment must be based on the blood urea concentration. When an exchange-transfusion has lowered it from 2 to 3 Gm. one may reduce the quantity of blood the next time (never less than 4 liters per adult) and space the transfusions.

As to the action of this treatment, the authors think that new blood does not act by simple substitution, but that it provokes the indispensable metabolism not only at the level of the kidney but also of the liver and the entire organism.

Miscellaneous

The international review of medicine and therapeutics *Le Monde Médical* has just resumed publication.

The Third International Congress of Acupuncture will take place in Paris June 3-5, 1949. The general meeting of the International Union against Cancer which was to take place in Paris in 1948 has been postponed to 1949, on a date not yet selected.

Death of Professor Bezançon

Professor Fernand Bezançon, a member for thirty years of the Académie Nationale de Médecine, recently died at the age of 80 years. A bacteriologist schooled by Chantemesse and Vidal, he was at the same time a pathologist, physiologist and, above all, a clinician.

Several of his works are classics. He devoted himself to the study of tuberculosis and its social repercussions. He succeeded Letulle at the Hôpital Boucicaut; he pursued experiments in social politics. He succeeded Léon Bernard at the Clinique de de Laënnec, and became the great master of French phthisiology.

He was the leading member of the Société de la Tuberculose, of the Comité National de Défense contre la Tuberculose and of the Commission on Tuberculosis at the Ministry of Public Health until his last days.

ITALY

(From Our Regular Correspondent)

FLORENCE, Sept. 30, 1948.

Blood and the Digestive Apparatus

At the National Congress of the Italian Association of Gastroenterologists, held in Chianciano under the chairmanship of Prof. Gasbarrini from the Medical Clinic in Bologna, reports were presented on the subject "Blood and the Digestive Apparatus." The speakers were Professors Marmont from the University of Genoa, Meneghini from Genoa and Torrioli from Rome. Marmont stated that consideration of the general phenomena of the vegetative sphere may demonstrate the necessity of an intercellular fluid endowed with at least three properties: (1) the vehicle for the nutritive substances, (2) sufficient supply of oxygen, and (3) removal of the refuse of cells. A thorough analysis has not been made of the importance of the elementary factors which take part in hemoplasmopoiesis. This problem may be of interest to the clinician in those cases in which it is uncertain at what point in the pathogenesis of disease the dietetic deficiency factor sets in and when the digestive change begins which causes the hemopathy. For erythropoiesis, vitamins, amino acid and mineral factors are considered necessary. The speaker stressed the importance of ascorbic acid, paraaminobenzoic acid, riboflavin and the so-called blood factors of the vitamin B complex. Three metallic elements, iron, copper and cobalt, are important in erythrogenesis. The predominant part is played by iron, which may be observed in ionizable form in the food. A deficiency of copper in the diet is responsible for a neuroanemic syndrome in sheep, and in human infants there is a characteristic hypercupremia associated with hyposideremia in infectious anemia. A deficiency of cobalt is the cause of an enzootic marasmus of cattle, while in man the administration of this metal may cause polyglobulism under normal conditions and may restore to normal the impaired erythropoiesis in tumoral or infectious anemia. One may distinguish three fundamental types of gastroenterogenic anemias: hyperchromic macrocytic, hypochromic mycrocytic and normocytic. The gastroduodenal factors are of primary importance in the determinism of the hypochromic microcytic, iron-deficient anemias. The speaker discussed iron-deficient chloranemia in women. He considers the concept of selective absorption, which has been emphasized by some American authors, as an unsufficient explanation, and he suggests the possible intervention of diencephalic neurovegetative factors which will provide a new orientation concerning chlorosis.

Professor Meneghini discussed the pathogenesis of anemias which follow gastric resection. Pernicious anemia resulting from a deficiency of the intrinsic factor may follow total removal of the stomach. Partial resection of the stomach may be followed by manifestations of pernicious anemia, or of mycrocytic hypochromic anemia, or even anemia of normocytic aregenerative type, which usually is normochromic. This last form may have its pathogenesis in a deficiency of a third gastric factor which stimulates erythropoiesis; this concept seems warranted by the results of animal experiments. The polyglobulism observed in patients with gastroduodenal ulcers has been interpreted as of gastrogenic origin. In view of the importance of the diencephalic centers in the pathogenesis of gastroduodenal ulcers and the existence of diencephalic polyglobulism, nervous centers for the pathogenesis of hyperglobulism must be admitted, but they may be influenced indirectly by an increased gastrohormonal activity.

Torrioli reported a series of studies concerning the relation of the alimentary canal to hemopoiesis. The starting point for these studies was the concept that pernicious anemia may be a disease with symptoms of multiple deficiencies among which there may easily be recognized a deficiency of the antianemic principle, of iron and of vitamin B. The complex problem may be clarified, in part, by the study and the complete examination of a large number of families whose members are affected by pernicious anemia. This work had been in progress at the Center for Blood Diseases in Rome. The speaker reported the following results of a two year follow-up on 200 families: (*a*) Hypochromemia with reduced absolute values of circulating hemoglobin and associated with hyperglobulism in some cases, has been the most frequent observation among relatives of patients with pernicious anemia. Anemia occurred most frequently in these persons as a sequela of any minimum pathologic cause, such as adenopathy and influenza. (*b*) The erythrocytometric curve is profoundly altered with multiform changes which may be related to three fundamental types as follows: deviation to the left, deviation to the right, enlarged and lowered curve or diphasic or flattened curve. (*c*) Oral disorders occur such as atrophy of the lingual mucosa or changes in the paradentium (familial dystrophic paradentiopathy). (*d*) Oligochylia occurs; this alteration may be less frequent and may not be present necessarily in persons who may present the other changes in a most pronounced degree.

The problem concerning anisocytosis is much more complex. According to the majority of authors, the erythrocytic curve will be restored to normal in patients who have recovered definitely from pernicious anemia, and it should therefore be considered as linked with a deficiency of the antianemic prinicple. Starting from this concept, the speaker and his co-workers concluded that patients who recovered from pernicious anemia did not present a normal erythrocytometric curve, but showed the fundamental changes which were observed in their parentage, after the disappearance of the megalocytic generation. The authors also concluded that the ground on which pernicious anemia may develop is characterized by a syndrome of a gastrointestinal lability which is manifested by a hypofunction of all the mucosae. But besides of this debility one must consider a hematic abnormality which is manifested by decisive alterations of the red cells and with a constant deficiency of circulating hemoglobin; i. e., one which predisposes a person to easy anemization resulting from inadequate causes. The speaker does not believe that it may actually be possible to establish that all these abnormalities may be considered as congenital, or that on the contrary they may be related only to gastrointestinal lability. A solution for these important problems may be achieved during subsequent development of these investigations.

BUENOS AIRES

(From Our Regular Correspondent)

Sept. 15, 1948.

Treatment of Cardiac Insufficiency by Ligating the Vena Cava

In a previous letter on the work of Pedro Cossio and J. Perianes (THE JOURNAL June 12, 1948, p. 659), reference was made to their experiments for relieving congestion of the lungs due to insufficiency of the left ventricle or mitral stenosis. In continuing the experiments, these authors attempted to reach their goal in two ways: (1) by accelerating the release of stagnated blood in the lesser circulation by anastomosing a pulmonary vein or a branch of the arteria pulmonalis with an extrathoracic vein or (2) by decreasing the amount of blood which passes through the right ventricle. They hoped to obtain this purpose (1) through tricuspid valvotomy and (2) through diminution of the venous blood coming back to the heart. At the beginning of the experiments, the vena cava inferior was narrowed in different degrees above the outlet of the venae suprahepaticae, but with little success. Almost all the animals

died because of thrombosis, intestinal infarcts or intrahepatic hemorrhages. It was difficult, indeed, to produce stenosis sufficient to diminish the pressure in the lesser circulation and at the same time not produce the aforementioned complications.

Ligation of the vena cava inferior above the suprahepaticae, reducing its lumen one-half, provokes an abrupt fall of the pressure in the right side of the heart and the arteria pulmonalis; on the other hand, ligation of the vena cava beneath the renales diminishes the pressure less, but more gradually, and does not provoke any functional disturbance.

As ligation of the vena cava has already been done for such other purposes as phlebothrombosis and thrombophlebitis after childbirth, it was decided to do it in cases of cardiac insufficiency which could not be controlled by medical treatment. The first attempt with local anesthesia in the zone of the incision failed because of violent pain provoked by detachment of the peritoneum. In 2 other cases general anesthesia with ether was used, but the operative accidents were so great that this method was abandoned, although the patients recovered and their cardiac condition was improved. Five more patients have been treated, all under local anesthesia, but this time combined with truncal anesthesia of the six or eight last intercostal roots and of the lumbar roots, and this with full success.

Before the operation, most of the patients were moribund. Two complications must be mentioned: phlebothrombosis and hypotension after the operation. Phlebothrombosis may be avoided by administering heparin or dicumarol for several days. The hypotension is more frequent. It is necessary to control the blood pressure during the whole operation and each hour afterward. It can be controlled by the Trendelenburg position and the usual analeptics. The results can be considered satisfactory. The dyspnea and the congestion diminish or disappear; the patient does not need to sleep sitting up; the venous pressure diminishes and does not rise when the lower extremities are elevated, and generally to further intensive medical treatment is not necessary.

However, the number of cases is yet too small for one to judge the value of this new procedure and to make definite interpretations.

Finally, the authors have ligated in animals all the great extrathoracic venous trunks with exception of the venae portae, affluentes and renales. The tolerance has been good. More cannot be said for the moment.

Sensitivity to Streptomycin

Drs. R. Cucchiani Acevedo and S. Erdstein reported to the Argentine Society of Tuberculosis observations among nurses who administer streptomycin to tuberculous patients. In 7 nurses, almost simultaneously, rosy and intensively pruriginous papules appeared on the fingers, sometimes preceded by erythema; later, vesicles developed with intense pruritus, swelling, perionyxis, vesiculation, fissures and desquamation. Later, the exanthem appeared with the same symptoms at the bend of the elbow; there was pruritus in both eyelids with sensation of drowsiness, periorbital edema, conjunctival congestion and photophobia. Similar phenomena have been observed in other institutions. The observations made by Rauchwerger and his co-workers (THE JOURNAL, Feb. 28, 1948) seem to be similar to those of the authors.

All the affected nurses had been in contact with the drug for many months, but the symptoms appeared only in the last eight weeks; it is therefore supposed that the hypersensitivity develops only after prolonged exposure to the drug. The localizations in the elbow and periorbital areas are explained by the fine nebulization which takes place when the injection is prepared by the nurses. Diphenhydramine hydrochloride ("benadryl hydrochloride") and "antistin" (2-[*N*-phenyl-*N*-benzyl-aminoethyl] imidazotin) did not give favorable results; however, autohemotherapy diminished the pruritus. Desensitization with 25 units of streptomycin intradermally produced pruriginous erythema with exacerbations when 50 units were injected.

As a prophylactic measure, some nurses prepare the solution and others inject it, using gloves and spectacles, avoiding the vapor by cooling the liquid before opening the bottle. Since then new cases have not been observed in the nurses. In 2 nurses not in contact with the drug for a month or so these manifestations disappeared completely but reappeared when they again were handling the drug.

The intradermal reaction should be carried out periodically with all the persons exposed to streptomycin, and a nurse should be temporarily withdrawn from the service when the first positive signs appear. It must be realized that patients treated with streptomycin might have such reactions when, after this medication has been stopped, the drug is readministered.

Number of Physicians in the Argentine

The National Direction of Investigations, Statistics and Census in Buenos Aires has published the results of a census of physicians and related professions in the Argentine in 1947. The sum total of practicing physicians is 18,301, 7,588 of whom practice in the capital, Buenos Aires, and 4,880 in the province of Buenos Aires. There are 6,643 dental surgeons. Seven hundred and twenty-five of the 3,548 midwives are in the capital, Buenos Aires.

Brief Items

Dr. Max A. Goldzieher, New York, gave several lectures in Buenos Aires, before the Argentine Medical Association, on the endocrine aspects of the arterial hypertension.

The Argentine Society for the Study of Sterility has been founded in Buenos Aires, similar to the societies already existing in other countries, under the chairmanship of Dr. Juan Carlos Ahumada, titular professor of gynecology. During the first session, in the Faculty of Medicine, Dr. John P. Greenhill (Chicago) addressed the audience on "Artificial Insemination."

The First Congress on Thoracic Surgery has been held in Buenos Aires under the chairmanship of the titular professor of this specialty, Dr. Jorge A. Taiana.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, Oct. 8, 1948.

Mannitol-Indole-Negative Members of Genus Shigella

In a recent paper, Dr. B. Rangel Pestana, of the Adolpho Lutz Institute, the central laboratory of the São Paulo State Department of Health, reports his study of several strains of Shigella dysenteriae that, contrarily to what is stated in Bergey's textbook, do not ferment raffinose and adonitol. A comparative study of S. dysenteriae strains and other mannitol-indole-negative organisms isolated from clinical cases of dysentery and similar to S. dysenteriae in morphologic, staining, cultural and biochemical characteristics, although serologically different, revealed, for the first time, the occurrence in São Paulo of Shigella sp. Sachs Q771. The practical value is obvious, for if this type is regarded, as it was until recently in several countries, as inagglutinable Shigella, the use of Shigella antiserum which would be recommended as the specific treatment would be of no value. Sorbitol and l-arabinose are the means to differentiate S. dysenteriae from Sachs type Q771, but the differentiation is not possible by morphologic, staining and cultural characteristics or by routine biochemical tests. S. dysenteriae fails to ferment any of those carbohydrates, while culture of type Q771 produces, as a rule slowly, an acid reaction. However, the only represen-

tative strain of Shigella sp. Sachs Q1167 examined by Pestana, which was received from the Connecticut State Department of Health, presented the same biochemical behavior as did Shigella sp. Sachs Q771, although they are serologically distinct; this proves the necessity of typing by means of specific serums. Unless the contrary can be shown by future investigations, the S. dysenteriae strains repeatedly observed by the author as well as strains of type Q771, when compared with those of Wheeler and Stuart, permit the differentiation, by means of l-arabinose, of S. dysenteriae from the Sachs indole-negative types, as the latter produce acid from this carbohydrate, whereas the contrary occurs with S. dysenteriae. The distinction between these types is based on serologic tests.

The Sachs types will introduce modifications in the present taxonomic systems. Borman, Stuart and Wheeler, in a detailed study on the taxonomy of the family Enterobacteriaceae, to which the Shigella genus belongs, speak of the probable immediate necessity of designating varieties in the non-mannitol-fermenting group, but express the opinion that it is still too early to determine the exact place of germs recently described as of the Sachs type. However, the paper by Wheeler and Stuart excludes from the genus Shigella some Sachs types and confirms the inclusion of the remaining strains, in this manner defining their taxonomic positions.

On the basis of his experiments, Pestana insists on the necessity of the routine use of cultures and S antiserums in agglutination tests. Beside many of the so-called inagglutinable Shigella organisms reported, which are, in fact, not S. dysenteriae, but Sachs indole-negative types, a greater number exists which owe their inagglutinability to the use of R forms instead of S forms. He also states that both the S and R forms of S. dysenteriae are toxic. Under the same conditions, neither S nor R strains of Shigella sp. Sachs Q771 showed toxicity.

Peritesticular Reaction in Leishmaniasis of Guinea Pig

In his studies of spontaneous leishmaniasis of the guinea pig, Dr. C. Magarinos Torres, of the Division of Protozoology of the Oswaldo Cruz Institute, Rio de Janeiro, disclosed that male guinea pigs given injections of Leishmania enriettii (saline suspensions of cutaneous lesions from another infected guinea pig) in the peritoneum showed curious changes in the tunica vaginalis. As a result of such changes, induration of the epididymis as well as the formation of a definite juxtatesticular nodule was observed, but without any involvement of the testis and the epididymis themselves. The histologic picture is rather complicated. In the early stages it resembles in some aspects the Shwartzman phenomenon, while certainly not identical to it, as could be easily inferred by the entirely different factors at work in the 2 cases. Later on and gradually the leishmaniotic granuloma containing a large number of parasites (L. enriettii) appears, accompanied by hemorrhages, thrombosis and suppuration, which are so prominent in the early stages. Further research is needed in order to establish the exact mechanism of this peritesticular reaction. The possibility of another infectious disease at work has not so far received confirmation.

Report on Patients with Heart Disease

Dr. Reinaldo Chiaverini reported a study of 429 patients with heart disease attended at the Misericordia Hospital of São Paulo. The causes were, in decreasing order of frequency, arterial hypertension in 31 per cent of the cases, coronary arteriosclerosis in 22 per cent, cardiovascular rheumatism in 16 per cent, syphilis in 13 per cent, American trypanosomiasis (Chagas' disease) in 7 per cent, pulmonary hypertension in 3 per cent, and other causes in 8 per cent. In more than one third of the cases there were several causes in the same patient, the association of arterial hypertension and coronary sclerosis (17 per cent), and syphilis and arteriosclerosis hypertension (6 per cent) being the most common. Cardioarticular rheumatism and American trypanosomiasis were the most frequent independent causes of heart disease, while arterial hypertension and coronary sclerosis were the most frequently associated causes, together or with other disease. The principal cause of aortic insufficiency was syphilis (63.5 per cent of the cases), followed by rheumatism (33.8 per cent) and other causes (2.7 per cent). In 22 cases (or 5.1 per cent) a severe, chronic myocardial disease was diagnosed of undisclosed cause. In only 12 cases (2.7 per cent) myocardial infarct was the cause of the trouble, which seems to indicate that this disease is not frequent in the economically lower part of the city population which is served by the Misericordia Hospital. Congestive cardiac failure was present in almost 90 per cent of the patients, while the most frequent disturbances of rhythm and conduction were branch block (12 per cent), auricular fibrillation (12 per cent) and different degrees of auriculoventricular block (3 per cent). The disease presenting the greatest tendency to disturb the conduction system of the heart was American trypanosomiasis, which caused auriculoventricular block in 10 per cent of the patients and branch block in 40 per cent. Rheumatic and sclerotic diseases of the heart were the most common causes of auricular fibrillation, being present in 21.4 per cent and 17.8 per cent, respectively.

Esophageal Electrocardiogram in Posterior Infarction

In view of the difficulties often encountered in the electrocardiographic diagnosis of old posterior infarction, multiple esophageal leads were taken by Drs. Aarão Benchimol, Paulo Schlesinger and Murilo Cotrim of Hospital Moncorvo Filho, Rio de Janeiro, in 11 patients in whom the presence of infarction was suggested by the usual standards and unipolar extremity leads or by a positive clinical history. The configuration of the normal esophageal electrocardiogram was studied in 3 patients, with particular reference to the shape of the QRS complexes recorded at the auriculoventricular transition. A classification of posterior infarction is presented according to extension and depth of myocardial involvement as judged by esophageal leads.

Although posterior infarction can usually be recognized by standard leads and the unipolar lead of the left leg, there are certain cases in which esophageal leads are required for a positive diagnosis. Multiple leads at various esophageal levels should always be taken, since an incomplete exploration may occasionally fail to reveal the presence of localized lesions of the posterior wall of the left ventricle.

An Unusual Case of Endometriosis

A case of endometriosis in a uniparous white Brazilian woman, aged 43, is reported by Prof. Clovis Corrêa da Costa of the Faculdade de Ciencias Medicas of Rio de Janeiro. The patient stated that since she was 25 she has noticed hard, painful nodules in the inner aspect of the thighs, which always got red before menstruation and finally bled. She also complained of dysmenorrhea. The nodules showed scarlike changes after menstruation, preceding new ones which appear soon afterward. About seven years ago similar formations appeared in the lower mammary grooves on both sides, on the pectoralis regions and neighborhood of the axillary plicae. Gynecologic examination showed retroflexed uterus with a small fibroid in its posterior aspect.

Reference is made by Prof. Corrêa da Costa to 2 other cases of external endometriosis, one on the internal aspect of the thigh and a similar case on the hand.

Correspondence

HEMORRHAGE FROM ESOPHAGEAL VARICES

To The Editor:—In the February 28 issue of THE JOURNAL, page 616, a paper entitled "The Hemorrhagic Tendency in Congestive Splenomegaly (Banti's Syndrome)" appears; this was first presented by Dr. L. M. Tocantins at the annual session of the American Medical Association, June 12, 1947. He referred to a case of hemorrhage from esophageal varices treated by tamponade at the Pennsylvania Hospital, Philadelphia, in May 1945.

Since this was apparently the first recorded instance of treatment by this method, I thought the enclosed photographs

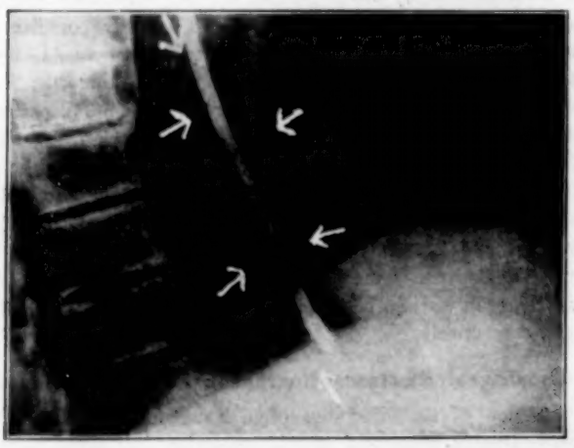


Fig. 1.—Oblique view of esophagus and cardia with balloon inflated.

of roentgenograms of the patient taken with the balloon in place might be of interest. Associates and I used a Miller-Abbott tube and balloon. Pressure was maintained by connecting the balloon to a mercury sphygmomanometer. The tube was held in place by a tie placed around the head and secured at the nares.

This was one of several cases of bleeding esophageal varices so treated at that time. In this small series of cases, as an emergency life-saving measure, it was of definite value.

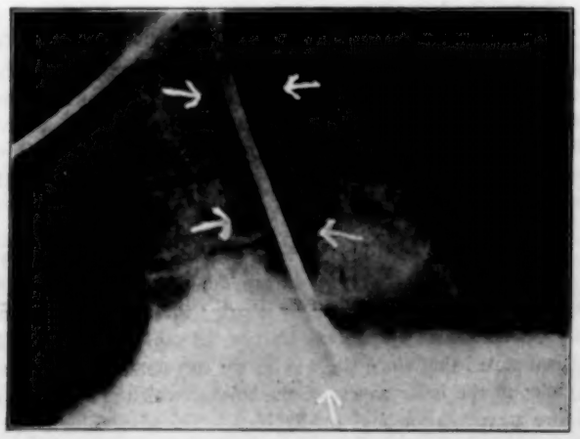


Fig. 2.—Lateral view of esophagus and cardia with the balloon inflated. The arrows indicate the air shadow of the inflated balloon in the lower end of the esophagus and cardiac end of the stomach.

The first patient was in extremis when treatment was instituted, and died six hours later. The second case was complicated by far advanced hemochromatosis, and the patient died two days following intubation. Both of these patients stopped bleeding, as evidenced by absence of blood on gastric suction. Both cases at post mortem showed evidence of esophageal varices and effective placement of the balloon. The third case is the one discussed by Dr. Tocantins. A fourth case, in a woman of 35 years, was diagnosed as Banti's syndrome complicated by bleeding esophageal varices. Her response was as dramatic as that in the third case. She left the hospital ten days after admission, asymptomatic.

Since returning from the service, we are at present enlarging our small series. Dr. Tocantin's modifications have been proving effective. In one case, a three lumen tube was passed so that tube feeding could be used while the balloon was in place. We hope to present this material as the subject of a report in the near future.

EDWARD W. BIXBY JR., M.D.,
Pennsylvania Hospital, Philadelphia.

CHLOROMYCETIN

To the Editor:—As you know, the October 9 issue of THE JOURNAL has an editorial on chloromycetin on page 432. The editorial states that "similar therapeutic effects were recorded with embryonated eggs infected with psittacosis virus, variola virus or influenza A virus." It further states that "chloromycetin was equally effective with mice infected with Japanese encephalitis." Both of these statements are incorrect. In their original paper Smadel and Jackson (*Science* **106**:418 [Oct. 31] 1947) stated that "chloromycetin has been ineffective in the treatment of mice infected with Japanese encephalitis and eggs infected with variola virus and influenza A virus. In another reference not quoted in the editorial (Smith and others, *J. Bact.* **55**:425 [March] 1948) chloromycetin was found to afford no protection against type A influenza, St. Louis encephalitis and fixed rabies virus infections in mice or in eggs.

I feel that it is important to call your attention to the errors in this editorial in order to avoid arousing false hopes on the value of chloromycetin in therapy of the virus diseases.

ALBERT MILZER, PH.D.,
Michael Reese Hospital,
Chicago.

Bureau of Investigation

AUGUST WAS BAD MONTH FOR HORMONE CREAM PROMOTER

On Aug. 4, 1948, Daniel Platt pleaded guilty to a criminal information containing twelve counts, each of which represented an alleged violation of the Food, Drug and Cosmetic Act of 1938, based on representations made by the defendant in the promotion of a so-called bust-developing cream which he called "Formalon." A federal judge thereupon sentenced him to prison for a total of three years on the twelve counts, but suspended the sentence. A fine of $250 was then assessed on each of the twelve counts, or a total of $3,000. In addition, the court ordered the defendant Platt to be placed on probation for a period of three years, there being included a condition that he remove himself completely from any business relating directly or indirectly to the manufacture and sale of any drug or food product.

More recently Platt has been promoting another hormone cream breast-developer. This one he called "Manogin." A circular put out by the Manogin Company in the promotion of this product was so bad that it was felt necessary to comment on it in THE JOURNAL under the auspices of the Council on Pharmacy and Chemistry.[1]

The Post Office Department now announces that it has invoked a fraud order against the Manogin Company and its officers and agents as such. Aug. 20, 1948, was the effective date of such fraud order. The findings of fact on which the fraud order was issued brought out by way of expert testimony the uselessness of this preparation because of the small estrogenic content, even though used over long periods of time.

1. "Manogin"—Another "Bust Developer," J. A. M. A. **137**:950 (July 10) 1948.

Council on Medical Education and Hospitals

Approval of the Chicago Medical School

The Chicago Medical School, located at 710 South Wolcott Avenue, was inspected by representatives of the Council on Medical Education and Hospitals and the Association of American Medical Colleges in October 1948. This inspection revealed that the Chicago Medical School offers an educational program that meets the Council's standards for an approved medical school. Accordingly, at its meeting on Nov. 9, 1948, the Council voted to admit the Chicago Medical School to its list of approved medical schools. By this action all students in regular attendance at the school on graduation will be considered by the Council to be graduates of an approved medical school. This action does not apply to students who completed their formal academic education at the school prior to Nov. 9, 1948 and who are now serving the year of internship required by the school before the degree of Doctor of Medicine is awarded. Likewise, this action does not affect the status of physicians who graduated from the school prior to Nov. 9, 1948.

On the same day that the Council voted to admit the Chicago Medical School to its approved list, the school was elected to membership in the Association of American Medical Colleges.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I & II.* Various Centers, Feb., June and Sept. 1949. *Part II.* April. 1949. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia 2, Pa.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* San Francisco, Feb. 8-10, 1949. Final date for filing application is Dec. 1, 1948. New York City, March 23-25. Final date for filing application is Jan. 2. Philadelphia, June 1-3. Final date for filing application is Jan. 2. *Written.* Oct. 17, 1949. Final date for filing application is May 1. Asst. Sec.-Treas., Dr. W. A. Werrell, 1 W. Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 1949. Final date for filing application is Jan. 1949. Sec., Dr. W. J. German, 310 Cedar Street, New Haven, Conn.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Jan. 14. *Oral.* San Francisco, March 21-24; New York, June 11-15; St. Louis, Oct. 15-19; Boston, Dec. Sec., Dr. S. J. Beach, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPEDIC SURGERY: *Part I.* Various Centers, April & May. Final date for filing application is Dec. 31. Sec., Dr. Francis M. McKeever, 1136 W. 6th St., Los Angeles 14.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, May 11-14; Chicago, Oct. 4-7. Sec., Dr. D. M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April. Final date for filing application is March 1. Sec., Dr. Robert A. Moore, 507 S. Euclid Ave., St. Louis 10, Mo.

AMERICAN BOARD OF PEDIATRICS: St. Louis, Feb. 18-20. Baltimore, April 22-24. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Rd., Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE: Atlantic City, June 4-5. Final date for filing application is March 15. Sec., Dr. R. L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec., Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF PSYCHIATRY & NEUROLOGY: *Oral.* May. Final date for filing application is Feb. 15. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March 1949. Final date for filing application is Dec. 1. Sec., Dr. J. S. Rodman 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Feb. 1950. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 18, Minn.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 28-30, 1949. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ALASKA: * Juneau, March 1. Sec.-Treas., Dr. W. M. Whitehead, Box 140, Juneau.

CALIFORNIA: *Oral.* Los Angeles, Nov. 20-21. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

COLORADO: * Denver, Jan. 4-7. Final date for filing application is Dec. 18. Sec.-Treas., Dr. W. W. King, 831 Republic Bldg., Denver 2.

DELAWARE: *Examination.* Dover, Jan. 11-13. *Endorsement.* Jan. 20. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

FLORIDA: * *Examination.* Jacksonville, Nov. 28-30. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O. San Francisco, Calif.

HAWAII: *Examination.* Honolulu, Jan. 10-13. Sec., Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu 53.

IDAHO: Boise, Jan. 10-12. Dir., Bureau of Occupational Licenses, Miss Estella S. Mulliner, State House, Boise.

INDIANA: *Examination.* Indianapolis, June 1949. Sec., Board of Medical Registration & Examination, Dr. Paul R. Tindall, 416 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 6-8. *Endorsement.* Des Moines, Dec. 6. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 15-16. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 13-15. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville 2.

LOUISIANA: *Examination.* New Orleans, Dec. Sec.-Treas., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans 12. *Homeopathic Examination.* Baton Rouge, subject to call. Sec., Dr. F. H. Hardenstein, 715 Pere Marquette Bldg., New Orleans.

MARYLAND: *Examination.* Baltimore, Dec. 14-17. *Endorsement.* At the discretion of the Board. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic Examination.* Baltimore, Dec. 7-8. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MISSISSIPPI: *Reciprocity.* Jackson, Dec. 6. Exec. Officer, State Board of Health, Dr. Felix J. Underwood, Jackson.

NEBRASKA: * *Examination.* Omaha, June. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Building, Lincoln 9.

NEW HAMPSHIRE: Concord, March 10. Sec., Board of Registration in Medicine, Dr. John S. Wheeler, 107 State House, Concord.

NEW YORK: *Examination.* Various Centers, Feb. 1-4. Sec., Dr. J. L. Lochner, Jr., 23 S. Pearl St., Education Bldg., Albany.

NORTH CAROLINA: *Endorsement.* Raleigh, Jan. 17. Sec., Dr. Ivan M. Procter, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 4-7. Act. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, Dec. 13-15. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OREGON: * *Examination.* Jan. 5-7. Final date for filing application is Dec. 22, 1948. *Endorsement.* Jan. 21-22. Final date for filing application is Jan. 3. Exec. Sec., Mr. Howard I. Bobbitt, 608 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia, Jan., 1949. Act. Sec., Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

PUERTO RICO: *Examination.* Santurce, March 1. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

SOUTH CAROLINA: *Endorsement.* Columbia, Dec. 6. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 18-19. Sec., Dr. G. J. Van Heuvelen, Capitol Bldg., Pierre.

UTAH: *Examination.* Salt Lake City, July. Sec., Dept. of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

VERMONT: *Examination.* Burlington, Feb. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: *Examination.* Charlotte Amalie, Dec. 8-9. Comm., Dr. Christian R. Moorhead, Charlotte Amalie.

VIRGINIA: *Examination.* Richmond, Dec. 3-4. *Endorsement.* Dec. 2. Sec., Dr. K. D. Graves, 30½ Franklin Road, Roanoke.

WASHINGTON: * Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WEST VIRGINIA: Charleston, Jan. 3-5. Sec., Public Health Council, Dr. N. H. Dyer, Capitol Bldg., Charleston 5.

WISCONSIN: * Madison, Jan. 11-13, 1949. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls, Wis.

WYOMING: *Examination.* Cheyenne, Feb. 7. Sec., Dr. Franklin D. Yoder, Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: Juneau, Feb. 21-26. Sec.-Treas., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: *Examination.* Tucson, Dec. 21. Sec., Mr. Francis A. Roy, University of Arizona, Tucson.

COLORADO: *Examination.* Denver, Dec. 1-2. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 3.

CONNECTICUT: New Haven, Feb. 12. Exec. Asst., State Board of Healing Arts, Miss Mary G. Reynolds, 110 Whitney Ave., New Haven 10.

MICHIGAN: *Examination.* Ann Arbor & Detroit, Jan. 14-15. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

MINNESOTA: *Examination.* Jan. 4-5, April, June and Oct. Sec.-Treas., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis.

OKLAHOMA: Spring of 1949. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. Sec., Basic Science Examining Committee, Dr. C. D. Byrne, Univ. of Oregon, Eugene.

SOUTH DAKOTA. *Examination.* Vermillion, Dec. 3-4. Sec., Dr. G. M. Evans, Yankton.

TENNESSEE: *Examination.* Memphis, Dec. 30-31. Sec., Dr. O. W. Hyman, 874 Union Avenue, Memphis 3.

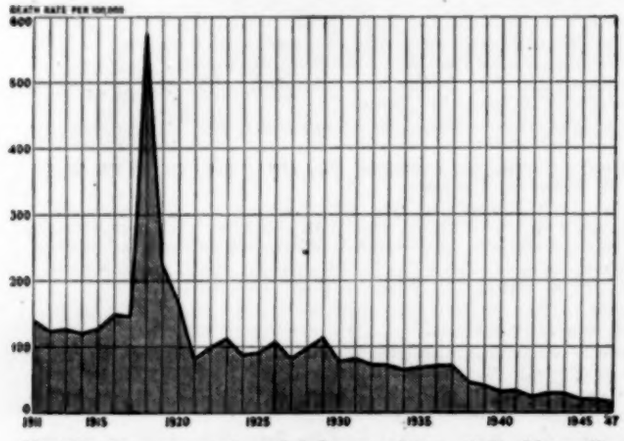
WASHINGTON: Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WISCONSIN: *Examination.* Milwaukee, Dec. 4. Final date for filing application is Nov. 27. Sec., Prof. W. H. Barber, Scott & Watson Sts., Ripon.

Miscellany

INFLUENZA AND PNEUMONIA—THIRTY YEARS AFTER THE PANDEMIC

Thirty years ago a worldwide epidemic of influenza struck the Atlantic seaboard and swept through the country in a general westerly direction along the main lines of transportation. It is estimated that about 20,000,000 persons in the United States were attacked, of whom 550,000 died. The explosive character of the outbreak is apparent from the chart, based on experience among the industrial policyholders of the Metropolitan Life Insurance Company. In 1918 the adjusted death rate from influenza and pneumonia among these insured (ages 1 to 74 years) was 575 per 100,000, or more than four times the average for the preceding seven years. During the last three months of the year, when the pandemic was at its height,



Mortality from pneumonia and influenza, 1911 to 1947; Metropolitan Life Insurance Company, weekly premium-paying business, ages 1 to 74. Annual death rates have been adjusted for changes in age, sex and color composition of these policy holders.

the death rate from these diseases, on an annual basis, was more than eleven times the rate for the preceding twelve month period.

In the years since the pandemic, however, phenomenal progress has been made in reducing the mortality from influenza and pneumonia. A new era was inaugurated in the early thirties, when specific serum treatment for many types of pneumonia was introduced. The death rate among these policy holders dropped from about 80 per 100,000 in 1930-1931 to about 70 per 100,000 in 1936-1937, during which period this type of therapy came increasingly into use. But just as the serum treatment was proving its worth in the battle against pneumonia, treatment with the sulfonamide drugs was introduced. In 1938, when both serum and the sulfonamide drugs were used, the death rate from pneumonia and influenza dropped sharply to 46.9 per 100,000 policy holders, a decrease of almost 35 per cent from the year before. The continued improvement in treatment with sulfonamide drugs and the introduction of penicillin brought still further success. By 1947 the rate reached the all-time low of 17.4 per 100,000; the rate for the current year will probably fall still lower. The efficacy of the newer methods of treatment is clearly evident from the fact that the improvement in mortality has been relatively three times as great in the past decade as in the preceding one.—*Statistical Bulletin*, Metropolitan Life Insurance Company, September 1948.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Pharmacists: Sale of Barbiturate Capsules Without Prescription; Liability for Suicide of Purchaser.—The plaintiff sued for damages for the death of her husband alleged to have been caused by the wrongful act of the defendant pharmacist. From a judgment in favor of the defendant the plaintiff appealed to the Supreme Court of South Carolina.

Section 5128-25 of the South Carolina statutes, which the defendant is charged with having violated, provides that any person, firm or corporation selling any of that general class of synthetic drugs, commonly known as barbiturates or their counterparts, except on the written prescription of a licensed physician, shall be deemed guilty of a misdemeanor. The plaintiff alleged that her husband, after having suffered from a cold and influenza, went to the defendant's pharmacy and asked for some drug which would "ease his nervousness and promote sleep." In response to this request the defendant sold him some barbiturate capsules in a box or container without any label showing the contents thereof and without first receiving a physician's prescription directing such sale. Thereafter, over a period of about a year, the defendant, at the request of the deceased, continued to sell him these capsules. The plaintiff then alleged that the barbiturate preparation in question was a habit-forming drug, that the deceased was not advised of its nature and that as a result of taking the capsules he became habituated to the use of the drug, in consequence of which he deteriorated mentally and physically. While under the influence of the drug, or while suffering from moroseness, caused by its habitual use, the deceased committed suicide by hanging. The plaintiff then concluded with the allegation that the capsules were sold to her husband in violation of the law and that his death by suicide was the proximate result of the wrongful acts of the defendant pharmacist in making such sales.

South Carolina law authorizes the representative of an estate to sue for damages for the wrongful death of a person if the wrongful act which caused such death would have entitled the deceased to maintain an action and recover damages in respect thereof during his lifetime. The defendant contended that the drug habit of the deceased was a direct consequence of his own voluntary act in taking the barbiturate capsules and not the result of the sale of the drug to him; that the consumption of the capsules was an act independent of and entirely distinct from the sale, depending entirely on the free will of the purchaser, and that the consumption and not the sale was the proximate cause of any resulting injury; that the deceased, by the exercise of ordinary care, might have escaped making himself a drug addict and by not doing so, he was the author of his own act. It was therefore urged that no cause of action accrued under the statute.

The court pointed out that the complaint set forth that the deceased, from time to time during a period of about a year, bought barbiturate capsules from the defendant and that at the end of said time he committed suicide by hanging himself. It is nowhere specifically alleged, said the court, that the deceased was incapable of consenting to any one or more of the sales of capsules or that the defendant had any knowledge that he was incapable or lacked volition in making such purchases. There is nothing to show that the deceased lacked self control or judgment or that he appeared to be under the influence of any drug when he applied for the capsules. We think, concluded the Supreme Court, that the inference is inescapable that the deceased knew the nature of the drug. He certainly must have known it after taking the capsules following his first purchase. He continued to make periodic purchases and the complaint alleges that he acquired the drug habit. But long before he became an addict he must have realized the effect the drug was having on him and if he had survived and brought this suit, he would not have been heard to say that he was not taking a "narcotic." His own contributory negligence would bar the action.

The defendant next argued that he could not be held liable on the theory of proximate cause. In every case of this

character, the Supreme Court pointed out, the inquiry is: Was the injury a natural and probable consequence of the wrongful act, and ought it to have been foreseen in the light of the attendant circumstances? In this case, the court continued, the deceased took his own life by hanging. Can it be reasonably said that his tragic end was a natural and probable consequence of the sale to him of the barbiturate capsules, and should it have been foreseen in the normal course of events? It might be that defendant should reasonably have foreseen that the deceased would become a drug addict but not that the deceased would kill himself. All that can be said is that the deceased's unlawful act could have produced a condition of mind out of which the tragedy could have resulted. However, so many elements may enter into a suicide that it is impossible to say that it was the natural and probable consequence of the negligence. In order to reach such a conclusion, continued the Supreme Court, we would have to eliminate entirely all those elements of feeling, temperament, disposition, emotional disorders, background and lack of self control, which might of themselves have been sufficient to bring about the tragic result, even though the person committing suicide had not been under the influence of a drug. While it may be true that some suicides may result from the excessive use of drugs, such as barbiturates, yet, as a vast majority of the persons who use this form of drug do not commit suicide, it could not be said that he who sells the drug may reasonably contemplate that suicide will follow. The voluntary wilful act of suicide of an uninjured person, who knows the purpose and physical effect of his act, is generally held to be such a new and independent agency as does not come within and complete a line of causation from the injury to the death so as to render the one responsible for the injury civilly liable for death. We think, the Supreme Court concluded, it would be going entirely too far in this case to hold that the unlawful sale of the barbiturate capsules brought about a condition of suicidal mania as the natural and probable consequences of the sale, or that this result should have been reasonably foreseen by the defendant. Accordingly the judgment of the trial court holding that the defendant pharmacist was not liable for the death of the plaintiff's husband, was affirmed. *Scott v. Greenville Pharmacy, Inc., 48 S. E. (2d) 324 (S. C., 1948).*

Workmen's Compensation Acts: Employee's Refusal to Cooperate with Physician.—The claimant commenced a proceeding to obtain an award under the workmen's compensation act for compensation for the loss of his leg. From a ruling against him by the Industrial Commission, the claimant appealed to the Supreme Court of Appeals of Virginia.

The claimant sustained an injury to his shin at the site of an old fracture and reported to the company physician on Sept. 16, 1946. The physician removed some necrotic tissue, applied an elastic bandage and told the claimant to return for further attention in two days. When he did not return as directed, Dr. Healy, the physician, went to the tool room where the claimant worked and tried to explain to him how serious the trouble was, because of the fact that the ulcer was superimposed on an old area of discolored skin caused by the previous fracture. The claimant was very indefinite and would not promise to come back. He did return, however, on October 18, at which time his leg was about in the same condition—still with an infected abrasion. He was again instructed to come back in two days, which he did. At that time the bandage applied by the doctor two days before had been removed and there was a badly soiled piece of cloth and some sort of grease on the wound, which the doctor cleaned off with ninol and ether. The claimant was again instructed to return two days later, but the doctor did not see him again until December 5, about six weeks later. At that time his leg was a little worse and the doctor again sought to impress on him the importance of having it attended to. In turn, the claimant tried to impress on the doctor how well he himself had been able to take care of other ulcers he had had on his legs, stating that he had had a similar accident in May and had cured it himself. He did not return to Dr. Healy for treatment after December 5. The leg was finally amputated by another physician about four months later.

Dr. Healy testified that he made every effort to induce the claimant to come to see him regularly but the claimant failed to do so. In addition to Dr. Healy's efforts, the shop foreman, at the request of the nurse in charge, told the claimant to go to the first aid room, but got no definite promise from him. Dr. Healy and the nurse called the claimant's immediate boss to see whether he could get him to come for treatment. The boss saw the claimant several times and told him to go. He testified that the claimant went some place, but whether he went to the first aid room he did not know. Torbert, a machinist, who was safety marshal and worked right at the tool room and who was a friend of the claimant, testified that on different occasions he was asked by the nurse, as a favor to her and to the claimant, to request the claimant to report for treatment. He did so, but the claimant did not go. He saw the claimant five different times. He and his father, who was a wholesale druggist, talked to the claimant several times about his leg. It seemed to be healing from the top, and the claimant was pulling the skin up from time to time to try to get healing from the bottom first. He asked Torbert whether he could get him a mixture of mutton tallow and turpentine. Torbert said that the claimant was trying to get cured all by himself and told Torbert he was not going to see the doctor and the nurse any more, as he could do more for his leg than they could.

The claimant did not contradict any of this evidence. His testimony was that he went to the first aid room as much as he could, which was eight or ten times, and that the reason he did not go oftener was because, as he expressed it, his job was at stake. On the other hand, there was evidence that permission to go for treatment could have been had at any time just for the asking. Furthermore, his immediate superiors, the doctor and the nurse, as well as his friend and co-worker, repeatedly urged him to go for treatment. The claimant did not testify that he ever made a specific request to go for treatment which was refused. Finally, Dr. Healy testified that if the claimant had come to him and taken treatments regularly he felt positive that his trouble would have been cured and that no amputation would have been necessary. There was no evidence of any kind to the contrary.

The Virginia workmen's compensation act provides that for a period not exceeding sixty days after an accident the employer shall furnish, free of charge, to the injured employee, such necessary medical attention as the nature of the accident may require, and the employee shall accept it, and during the remainder of disability, the employer may furnish, free of charge, an attending physician whom the employee shall accept, with certain exceptions and additions not involved in the present case. The law then goes on to provide, "The refusal of the employee to accept such service when provided by the employer shall bar said employee from further compensation until such refusal ceases, and no compensation shall at any time be paid for the period of suspension unless, in the opinion of the industrial commission, the circumstances justified the refusal, in which case the industrial commission may order a change in the medical or hospital service."

The questions presented by this appeal, said the Supreme Court of Appeals, are whether the employer furnished adequate medical services and attention and whether the claimant refused to accept them to such an extent as to bar him from compensation. On the basis of the evidence herein reviewed, the court was of the opinion that the claimant refused the medical attention offered him and urged on him, without any excuse for doing so other than his notion that he could take care of himself. This was not a legal excuse, said the court. The duty of the employee to accept such necessary medical attention as the nature of the accident may require is made compulsory by the statute. His refusal to do so, by like mandate of the statute, bars him from compensation until such refusal ceases. To have that consequence his refusal must be unreasonable and without just cause. The Industrial Commission found that "the preponderance of the evidence shows that all the complications which led to the amputation were due to his lack of cooperation and inexcusable refusal to receive the medical attention tendered him." This finding, concluded the Supreme Court of Appeals, is amply supported by the evidence. Accordingly the judgment of the Industrial Commission was affirmed and the employee was denied any compensation because of his failure to cooperate with the attending physician. *Stump v. Norfolk Shipbuilding & Dry Dock Corporation, 48 S. E. (2d) 209 (Va., 1948).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

36:1-160 (July) 1948

New Contributions to Study of Intracavity Potential in Cases of Right Bundle Branch Block in Human Heart. D. Sodi-Pallares, P. Thomsen and J. Soberon.—p. 1.
Effect of Dicumarol on Heart in Experimental Acute Coronary Occlusion. H. L. Blumgart, A. S. Freedberg, P. M. Zoll and others.—p. 13.
*Incomplete Division of Atrioventricular Canal with Patent Interatrial Foramen Primum (Persistent Common Atrioventricular Ostium): Report of Five Cases and Review of Literature. H. M. Rogers and J. E. Edwards.—p. 28.
Interpretation of Electrocardiogram in Dextrocardia with Situs Inversus. E. M. Shepard and H. J. Stewart.—p. 55.
Study of Alleged Intercoronary Reflexes Following Coronary Occlusion. D. F. Opdyke and E. E. Selkurt.—p. 73.
*First Ten Years of Rheumatic Infection in Childhood. Rachel Ash. —p. 89.
Axis Deviation in Human Bundle Branch Block. A. M. Jones and H. Feil.—p. 98.
Multiple Channel Electronic Stethoscope for Teaching and Demonstration. J. S. Butterworth and C. A. Poindexter.—p. 112.
Diagnostic Value of Pattern T_1 Lower Than T_3 ($T_1 < T_3$) Compared with Information Yielded by Multiple Chest Leads in Myocardial Infarction. W. Dressler and H. Roesler.—p. 115.
Further Studies on Effect of Papaverine on Cardiotoxic Lesions of Digitalis in Dog. F. A. Kyser and Ruth Trump.—p. 133.
False Abnormality of Precordial Electrocardiograms Due to Effect of Changes of Potential at Remote Electrode. E. Hull, H. D. N. Tucker and J. O. Weilbacher.—p. 135.
Simple Method of Determining Abnormalities of Q-T Interval. E. Goldberger.—p. 141.

Division of Atrioventricular Canal.—Rogers and Edwards report 5 cases of congenital cardiac disease termed incomplete division of the atrioventricular canal with patent interatrial foramen primum (persistent common atrioventricular ostium) and review the pathologic and clinical features in an additional 50 cases reported in the literature. In the entire group of 55 cases, the median age of the patients at the time of death was 10 months. More than half of the patients died before they were 1 year of age. Only 5 of the patients lived beyond the age of 30 years. The lesion under consideration acts essentially as does a simple interatrial septal defect. Enlargement of the right side of the heart and widening of pulmonary artery orifice are common secondary lesions. Cyanosis may be present at birth, but is usually acquired. When this manifestation develops, it is a sign of failure of the right side of the heart, pulmonary disease, or both. Cardiac murmurs, usually systolic, are frequently observed. Mongolism is a relatively common associated finding.

Rheumatic Infection in Childhood.—At the Children's Hospital of Philadelphia a register has been kept of all patients treated for rheumatic infection since 1922. In 1946 and 1947, a survey was made of all patients whose primary manifestation had occurred during the years 1923 to 1937, inclusive. Although many had been followed for much longer periods, the discussion is limited to the first ten years following the initial illness. At the termination of the initial attack 59.2 per cent of 547 children who were followed for ten years showed evidence of rheumatic heart disease. Of 219 patients with no clinical evidence of heart disease at termination of their first attack, 76.7 per cent still showed no evidence of heart disease ten years after onset. Only 5 per cent of this group with potential heart disease at onset had died of rheumatic infection or bacterial endocarditis. Of 318 patients with rheumatic heart disease at onset, 30 (9.4 per cent) showed disappearance of signs of cardiac involvement. Of this group with rheumatic heart disease at onset, 42.1 per cent had died of rheumatic infection or bacterial endocarditis. The most significant prognostic factor, so far as the initial illness is concerned, is related to the presence or absence of signs of cardiac damage. Chorea at onset is relatively benign, because it is less likely to be associated with carditis than is polyarthritis or other types of rheumatic infection. Ten years after onset, 60.3 per cent of these rheumatic patients were leading a normal existence. Those without clinical evidence of heart disease at the termination of the initial attack accounted for the majority of those presenting no functional incapacity. Twenty-four and four-tenths per cent of the total group had died of rheumatic infection, the predominant number of deaths occurring among those in whom a diagnosis of rheumatic heart disease had been made after recovery from the first attack. Death had occurred in only 5 per cent of the group in whom an original diagnosis of potential heart disease had been made, in comparison with a death rate of 42 per cent among those given a diagnosis of rheumatic heart disease at onset.

American J. Obstetrics and Gynecology, St. Louis

56:1-204 (July) 1948

Effectiveness of Various Diuretic Agents in Causing Sodium Excretion in Pregnant Women. W. E. Brown and J. T. Bradbury.—p. 1.
Mesonephric Remnants in Cervix. J. W. Huffman.—p. 23.
Abdominal Colpocystopexy for Complete Prolapse of Vagina and Bladder; Rectus Suspension Principle of Crossed-Suspender Support. P. F. Fletcher.—p. 41.
Cesarean Section in Detroit During 1945—Comparison with 1925 and 1930. H. C. Mack and R. S. Siddall.—p. 60.
Serum Beta-Glucuronidase Levels During Toxemia of Pregnancy. L. D. Odell and D. F. McDonald.—p. 74.
Face Presentation: Study of 160 Cases. J. W. Reddoch.—p. 86.
Review of 300 Anterior and Posterior Colporrhaphies with Plea for Anatomic Correction of These Traumatic Hernias Earlier and with Presentation of Author's Procedures of Repair. W. O. Johnson. —p. 100.
Changing Concepts in Cervical Biopsy. K. E. Cox, V. B. Buhler and W. C. Mixson.—p. 112.
Vaginitis Emphysematosa. H. L. Gardner.—p. 123.
Puerperal Inversion of Uterus. H. Henderson and R. W. Alles.—p. 133.
*Acute Anterior Poliomyelitis in Pregnancy. E. S. Taylor and J. M. Simmons Jr.—p. 143.
Prolapse of Vagina Following Abdominal Hysterectomy. D. A. Bickel. —p. 152.
Treatment of Urinary Tract Infections with Sulfathalidine (Phthalysulfathiazole). C. G. Johnson, L. H. Lorenzen and Ruth Y. Mayne. —p. 160.
Postmaturity. L. A. Calkins.—p. 167.
Surgical Management of Incomplete Abortion. W. S. Morse.—p. 173.
Amebic Vaginitis. B. Bernard Weinstein and J. C. Weed.—p. 180.
Treatment of Trichomonas Vaginalis with Tyrothricin. C. G. Johnson, J. W. Douglas and Ruth Y. Mayne.—p. 184.
Krukenberg Tumor with Osteoplastic Metastases. J. H. Zeigerman. —p. 187.
*Massive Gastric Hemorrhage in Pregnancy. J. Carangelo and T. D. Efstation.—p. 191.

Acute Anterior Poliomyelitis in Pregnancy.—Taylor and Simmons found that during the 1946 epidemic of poliomyelitis in Colorado the pregnant woman was twice as vulnerable to the virus disease as the nonpregnant woman of the same age group. Women in all months of pregnancy were equally susceptible to poliomyelitis. During the first two trimesters the prognosis for recovery is excellent. Poliomyelitis acquired during the last trimester carries a serious prognosis with respect to survival of the mother or escape from severe permanent paralysis. Estrogen and progesterone may be protective to a victim of poliomyelitis early in pregnancy. This is not true in the last trimester. The virus does not pass the placental barrier. All children born of mothers infected during this epidemic have been free from congenital disease. Management of pregnancy accompanied by acute poliomyelitis in the last trimester of pregnancy is a challenging problem. In the acutely ill patients, cesarean section seems unreasonable. Poliomyelitis had no ill effects on the progress of labor except that it necessitated an occasional forceps operation.

Massive Gastric Hemorrhage in Pregnancy.—Carangelo and his associates present the histories of 4 women who present the unusual complication of massive hemorrhage during pregnancy at term. Three presented an eclamptic syndrome of hypertension, edema, convulsions, oliguria and albuminuria. All 4 had severe projectile vomiting of blood, followed by marked decrease of blood pressure. In all, the onset of labor occurred twenty-four to twenty-eight hours following the onset of projectile hematemesis. Three of the patients were delivered of stillborn infants in whom the heart tones were not audible, following the onset of hematemesis. In 1 case, in which the mother survived, the infant was premature and viable. Patho-

logic study of case 1 revealed no specific source of hemorrhage in the esophagus or stomach in the form of varices. Superficial ulceration of the mucosa of the stomach and esophagus was noted. This may have been a source of bleeding, but it was not thought that it would have produced the amount of hematemesis noted clinically. The elevated temperature was probably due to the severe chronic endometritis in which there were necrosis and masses of bacteria in the endometrium. Together with this infection she had acute pyelonephritis bilaterally and an acute splenic tumor. This infection may have been the underlying cause of her massive hematemesis and the death of the fetus.

American Journal of Ophthalmology, Cincinnati

31:773-914 (July) 1948

Dacryocystitis of Infancy. J. V. Cassady.—p. 773.
Anatomic Factors in Etiology of Heterotropia. R. G. Scobee.—p. 781.
Review of 100 Cases of Retinal Detachment. Ruth Appleby and D. K. Pischel.—p. 796.
Problems in Research in Orthoptics. F. Elizabeth Jackson.—p. 805.
Agnostic Alexia Without Agraphia Following Trauma. H. H. Joy.—p. 811.
Widening of Angioscotoma in Alarm Reaction. M. R. Cholst.—p. 821.
*Character of Nystagmus Induced by Amytal in Chronic Alcoholics. M. B. Bender and C. A. Brown.—p. 825.
Diathermy Treatment of Angioma of Retina. P. M. Lewis.—p. 829.
Glaucoma Associated with Subluxation of Lens in Several Members of Family. J. P. Harshman.—p. 833.
Ocular Effect of Several Irritant Drugs Applied Directly to Conjunctiva. J. J. Estable.—p. 837.
Some Aspects of Studying Binocular Vision. K. C. Swan.—p. 845.
Further Experiences with Integrated Eyes and Vitallium Implants. W. L. Hughes.—p. 854.

Nystagmus Induced by "Amytal" in Chronic Alcoholism.—While studying the effect of barbiturates on eye movements Bender and Brown observed that in chronic alcoholic addicts intravenous injection of "amytal sodium" (sodium isoamylethylbarbiturate) produced fine, shimmering nystagmus instead of the coarse and slow nystagmoid movement which is generally seen in barbiturate intoxication of persons not addicted to alcohol. Comparative tests were made on 15 alcoholic addicts and 15 controls not addicted to alcohol. A 5 per cent solution of "amytal sodium" was injected into the antecubital vein at a rate not exceeding 0.1 Gm. or 2 cc. per minute. The total dose was never more than 0.5 Gm. or 10 cc. During these tests the patients were instructed to fix their gaze on an object away from the central visual axis. In the control subjects injection of "amytal sodium" generally produced ocular responses of two types: (1) wide, slow irregular oscillations in which the eye drifted slowly toward the midline from a point of fixation and returned to the original position with a flick, and (2) coarse, slow rhythmic nystagmus. All patients addicted to alcohol showed fine shimmering nystagmus. In 1 patient the type of nystagmus helped the discovery that the patient had been an alcoholic addict, which he had denied at first. It appears that if alcohol is imbibed over a long period, it alters the function of the nervous system. The fine rapid nystagmus is found even months after the patient has stopped drinking. This suggests that alcohol produces a more or less permanent change in nervous system function.

Amercian Journal of Public Health, New York

38:915-1060 (July) 1948. **Partial Index**

What's Happening to Malaria in the U. S. A. J. M. Andrews.—p. 931.
Some Labor Union Enterprises in Public Health Economics. B. A. Kogan.—p. 943.
International Population and Vital Statistics. F. E. Linder.—p. 951.
General Atmospheric Pollution: Air Pollution Control Program in Cleveland. H. G. Dyktor.—p. 957.
Id.: Some Work in Pittsburgh Air Pollution Problems. S. B. Ely.—p. 960.
Id.: Los Angeles "Smog." C. L. Senn.—p. 962.
Id.: New York City's Atmospheric Pollution Control Problems. A. C. Stern.—p. 966.
Medical Attendance During Terminal Illness. Marta Fraenkel.—p. 970.
Theoretical Considerations Concerning Caries Control. L. S. Fosdick.—p. 977.
Health Department Experience for School Health Coordinators in Washington. Marjorie Eastabrooks and H. Lundy.—p. 982.
Environmental Health Problems Related to Urban Decentralization. L. M. Board and H. J. Dunsmore.—p. 986.
Increasing Scope of School Sanitation Service in Local Department of Health Programs. S. D. Sturkie.—p. 997.

Annals of Western Medicine and Surgery, Los Angeles

2:241-288 (June) 1948. **Partial Index**

Corneal Lens—New Type of Plastic Contact Lens. Preliminary Report. M. W. Nugent.—p. 241.
*Streptomycin Toxicity. J. D. Davis, C. W. Anderson and A. E. Landy.—p. 245.
Vagotomy. Evaluation of Experimental Work, Research, Clinical Application and Results of Vagotomy in Various Clinics, with Statistics on 53 Vagotomies Performed at Los Angeles County General Hospital. A. M. Hansen.—p. 249.

Streptomycin Toxicity.—Davis and his co-workers report 117 patients who received streptomycin for some form of tuberculosis at the thoracic diseases service of the Birmingham Veterans Administration Hospital from January 1947 to January 1948. Streptomycin is considered sufficiently toxic to warrant recommending that it be administered only during hospitalization. Neurotoxic, anaphylactic, renal and general toxic reactions have been noted. Treatment was abandoned in 12 of the 117 patients because of severe toxic reaction after twelve to one hundred and five days of therapy. Of 105 patients who received 2 Gm. streptomycin for sixty to one hundred and twenty days 97 per cent manifested damage in the vestibular portion of the eighth cranial nerve, in which the neurotoxic selection by streptomycin is noted especially. In general, the onset of damage to the vestibular apparatus depends on the total amount of streptomycin received. Toxic effects on the cochlear portion of the eighth cranial nerve were relatively minor. Loss of hearing, chiefly in the high audiometric range, occurred in only 25 per cent of the patients. Loss of hearing in the audible range was noted in less than 3 per cent of the patients. More than 4 per cent eosinophils were noted in 78 of the 117 patients. In 18 correlation between good results of therapy and a high eosinophilia was noted, but 15 patients also obtained good results without eosinophilia, and in 8 patients with high eosinophilia poor results were observed. Leukopenia developed in 2 patients at the end of the sixty day regimen of treatment. A definite relation exists between the severity of toxic reactions and high levels of streptomycin in the blood.

Archives of Dermatology and Syphilology, Chicago

57:281-402 (March) 1948

Folliculitis Ulerythematosa Reticulata. G. M. MacKee and A. C. Cipollaro.—p. 281.
*Recurrent Lupus Vulgaris Following Surgical Excision and Replacement Skin Graft. S. S. Robinson and S. Tasker.—p. 293.
"Repeat" Cultures in Dermatophytosis. F. D. Weidman and F. A. Glass.—p. 300.
Studies on Sensitivity to Plasticizers: Ortho-Nitrobiphenyl, N-Isopropyl Benzene Sulfonamide and N-Isopropyl Benzene Sulfonamide and N-Isopropyl Ortho and Para Toluene Sulfonamide. Helen R. Gottschalk and R. S. Weiss.—p. 304.
*Effects of Topical Applications of Diphenhydramine Hydrochloride (Benadryl). T. H. McGavack, P. Schulman, R. Schutzer and H. Elias.—p. 308.
Herpes Zoster Associated with Monocytic Leukemia. S. M. Bluefarb.—p. 319.
Distrophia Unguium Mediana Canaliformis. M. M. Robinson and F. D. Weidman.—p. 328.
Myoepithelial Sweat Gland Tumor, Myoepithelioma: Report of 3 Cases with Review of Literature. W. F. Lever.—p. 332.
Dermatologic Evaluation of Yeast, Tyrotyricin, Chlorophyll and Nitrofurazone. H. A. Johnson.—p. 348.
Dermatitis of Hands. B. H. Winston.—p. 357.
Serologic Conflict: Study of Serodiagnostic Discrepancies. Bettina B. Carter.—p. 368.
Biologic Basis of Psychosomatic Disease of Skin. M. J. Brunner.—p. 374.
Leukoderma Acquisitum Centrifugum. M. Leider and T. M. Cohen.—p. 380.
Chemistry of Palmar Sweat. W. C. Lobitz and H. L. Mason.—p. 387.

Recurrence of Lupus After Skin Grafting.—Robinson and Tasker present the case of a woman, aged 50, who had had a lupus vulgaris lesion on the right cheek; the lesion had been excised and the area covered by a free thick skin graft. Although at first an excellent cosmetic result was obtained, about a year later there were signs of recurrence of the disease in the skin graft and scar. A review of the medical literature shows that despite the favorable reports from European investigators, frequent postoperative recurrences of the disease are observed in the United States. Since lupus vulgaris is frequently hematogenous in origin, the authors advise that if local surgical treatment is employed it should be combined with treatment for systemic tuberculosis.

Topical Application of Diphenhydramine.—According to McGavack and his associates diphenhydramine hydrochloride ("benadryl") has a powerful antihistaminic effect. The frequency of the side effects of the drug when given in adequate amounts by mouth has led to the investigation of its topical use for diseases in which cutaneous manifestations of a probably allergic nature are present. Topical application of 2 and 5 per cent concentrations of diphenhydramine in ointment bases in 63 patients reduced or completely destroyed the response of the skin to intradermally applied histamine. "Carbowax 1500" monostearate, an oil in water emulsion, appeared to be the best of the three bases employed. Seventy-four patients with itching dermatoses were treated with ointments containing diphenhydramine. Forty-four obtained complete relief from the itching, while an additional 18 were improved. Six patients experienced some discomfort from the application of the ointment, particularly when a 5 per cent concentration was used. In 4 of these patients this lasted not more than five minutes. Of the other 2, it was due to the base employed in one and to an aggravation of a weeping eczematous disease in the other. No systemic side reactions were observed in any of the 137 patients who were subjects of this study.

Archives of Internal Medicine, Chicago

81:115-248 (Feb.) 1948

Renal Arteriovenous Anastomoses in Rabbits, Dogs and Human Subjects. B. Simkin, H. C. Bergman, H. Silver and others.—p. 115.
*Thrombosis as Complication of Internal Diseases. S. Kallner.—p. 126.
*Hypoprothrombinemia: Effect of Transfusions of Blood Fortified by Administration of Vitamin K to Donors. H. R. Butt, T. B. Magath and T. H. Seldon.—p. 131.
Intravenous Administration of Mercurial Diuretics in Man: Immediate Effect on Electrocardiogram. L. Wolff and E. S. Sagall.—p. 137.
Meningococcic Bacteremia. W. B. Daniels.—p. 145.
Regulation of Pulmonary Arterial Blood Pressure. G. Liljestrand. p. 162.
*Carcinoma of Pancreas: Diagnostic Criteria. G. F. Dashiell and W. L. Palmer.—p. 173.
Association of Spontaneous Hypoglycemia with Hypocalcemia and Electro-Cerebral Dysfunction. M. Fabrykant and B. L. Pacella. p. 184.
Dynamics of Action of Penicillin: Time-Dose Relationship in Human Streptococcic Disease. E. Jawetz.—p. 203.
Cardiovascular Diseases: Review of Significant Publications from January 1944 to June 1947. O. Paul, with the editorial assistance of E. F. Bland and P. D. White.—p. 209.

Thrombosis and Internal Diseases.—Kallner emphasizes that in patients with pneumonia the temperature sometimes does not return to normal but remains subfebrile. The possibility of thrombosis must be considered. The appearance of blood-streaked sputum in these cases is probably a sign of pulmonary embolism pointing to the existence of thrombosis. In 3 such cases anticoagulant therapy with heparin and "dicumarol" produced rapid recovery. Heparin has been used in an instance of anuria caused by a hemolytic reaction after blood transfusion. Two hours after heparin was given the anuria cleared up. Heparin has also been successfully used together with ephedrine in cases of fibrinous bronchitis.

Hypoprothrombinemia: Administration of Vitamin K to Blood Donors.—This study by Butt and his associates was undertaken to repeat Kinsey's observation in cases of severe hepatitis with hemorrhagic manifestations which could not be controlled by administration of vitamin K or transfusion of whole blood. In attempting to control the hemorrhage, Kinsey administered 18 mg. of vitamin K intramuscularly to donors twenty-four hours prior to withdrawal of blood for transfusion. He reported that such blood, when administered to bleeding patients who did not respond to the usually effective measures, caused cessation of hemorrhage and increase in the level of prothrombin in four hours. Butt and his associates report observations on 3 patients in whom severe hepatic damage was accompanied by deficiency of prothrombin in the circulating blood. They found that prothrombin deficiency cannot be corrected by administration of vitamin K or of whole blood. It also has been shown that administration of so-called fortified blood is not effective in altering the prothrombin level in these patients. Not only was fortified blood of no value in correcting prothrombin deficiency in these patients with severe intrahepatic disease but, likewise, it was ineffectual in the correction of the deficiency in external biliary obstruction, in spite of the fact that the latter condition was quickly remedied by the administration of vitamin K alone.

Carcinoma of Pancreas.—Dashiell and Palmer analyze 90 cases of carcinoma of the pancreas. Pain is an extremely important and early symptom. It was present in 75 of the 90 patients, in all of the 50 in whom there was no jaundice and in 45 of the 60 in whom jaundice was present. The pain, although variable in character, was typically dull and persistent and located high in the abdomen, but occasionally it was referred to the lower part of the abdomen. It was primary in the back in 14 cases and radiated to the back in 22 cases. Jaundice was present in 60 of the 90 patients. In 35 of those with jaundice, the gallbladder could be palpated preoperatively. An epigastric mass was noted in about one third of the patients. Progressive and rapid loss of weight is extremely significant; it occurred in at least four fifths of their cases. Persistent anorexia is of similar importance. Persistent unexplained diarrhea, particularly steatorrhea occurring with abdominal pain, is suggestive of pancreatic neoplasm. Glycosuria, usually inconstant, occurred in 24 of the cases; a diabetic type of dextrose tolerance curve was found in 18 of 21 patients tested. The diagnostic value of this procedure may be greater than has been realized in the past. Roentgen signs of diagnostic importance were noted in nearly half of the series. Greater attention should be paid to the possibilities of roentgen examination as a diagnostic procedure. While there are no pathognomonic criteria for pancreatic neoplasm and the clinical picture is somewhat variable, the essential features are so definite and the procedures mentioned so helpful that the diagnosis should be made earlier and more accurately than at present.

Archives of Otolaryngology, Chicago

47:239-378 (March) 1948

Audiometric Studies of Residual Hearing of Pupils of Rio de Janeiro National Institute for the Deaf: I. Auditory Acuity of Deaf Children. A. P. Lacerda and A. E. Vervloet.—p. 239.
Id.: II. Study of Progress of Impairment of Children's Hearing. A. P. Lacerda and A. E. Vervloet.—p. 264.
Bone-Dust-Free Lempert Fenestra Nov-Ovalis: A New Evolutionary Development of Surgical Treatment of Clinical Otosclerosis. J. Lempert.—p. 280.
*Newer Concept of Management of Otogenic Infection. M. B. Hayes and C. F. Hall.—p. 289.
Loss of Speech Due to Meningitic Deafness. C. E. Kenney.—p. 303.
Peroral Endoscopy: A Review of the Literature for 1946. L. C. Clerf, J. T. Spencer and C. D. Riggs.—p. 337.

New Management of Otogenic Infection.—Hays and Hall show that in the temperate zone otogenic infections are essentially of two types, a winter type, infections due to gram-positive organisms, and a summer type, infections due to gram-negative organisms. The type caused by gram-positive organisms can be treated adequately with the sulfonamide drugs and the antibiotics. The type characterized by gram-negative organisms does not respond to these drugs. One hundred cases were studied clinically and bacteriologically (160 cultures). It was found that the resistant etiologic agent in chronic suppurative otitis media and external otitis was predominantly Pseudomonas aeruginosa (Bacillus pyocyaneus). In a carefully controlled bacteriologic and clinical study of 100 cases of otitic infections, a new chemical agent, dibromosalicylaldehyde, has been found more satisfactory than other agents suggested thus far. Owing to the unavailability of streptomycin, no opportunity has been afforded to study the efficacy of this antibiotic in these types of aural infections. Dibromosalicylaldehyde ("dalyde") is a readily available, inexpensive chemical agent, which is effective against both bacteria and fungi. It can be utilized in powder, ointment and solution. Seventy-one patients with external otitis were relieved of symptoms within twenty-four hours. In 30 the infection resolved in one week or less, and the rest required two to four weeks' treatment. Although follow-up was inadequate, only 1 patient returned with a recurrence; this one had seborrheic dermatitis. Of 28 patients who had otitis media, 12 had dry ears in two to six weeks; the remainder required up to two and a half months' treatment. Only in 8 did the ears fail to become dry.

Bulletin of Johns Hopkins Hospital, Baltimore

83:1-118 (July) 1948

*Virus, Nerve Cell and Paralysis: Study of Experimental Poliomyelitis in Spinal Cord. D. Bodian.—p. 1.

Virus, Nerve Cell and Paralysis.—Bodian says that published observations on the histopathologic changes in the spinal cord in poliomyelitis are numerous but the complexity of the problems of pathogenesis has resulted in contradictory interpretations and has left many points unsettled. It was felt that some of the important points remaining at issue perhaps could be investigated more satisfactorily by means of an approach which attempts to correlate pathologic processes in chronologic sequence, with changes in level of virus activity on the one hand and changes in clinical function on the other. It was felt that such an approach requires at least approximate quantitative data at all three levels of observation, and could therefore be essayed only in the experimental animal. In this extensive report Bodian gives a description of the course of a poliomyelitic infection in the spinal cords of rhesus monkeys killed at intervals from the preparalytic period to the chronic stage.

Canadian Medical Association Journal, Montreal

59:1-76 (July) 1948

*Treatment of Early Syphilis by Five-Week Penicillin-Mapharsen-Bismuth Schedule. A. Marin, F. L. Boulais, A. Lambert and others.—p. 1.
Problem of Older Age Hernia. H. I. Jackes, H. R. Robertson and W. H. Sutherland.—p. 7.
Psychology of Reconstructive Surgery. J. H. Couch.—p. 10.
Value of Splenectomy in Hematologic Disorders. C. W. Holland.—p. 13.
Estimation of Hearing Losses for Purposes of Adjudication of Disability Claims. A. E. Lundon.—p. 18.
*Rutin in Hematuria of Congenital Polycystic Disease of Kidneys. H. O. Foucar.—p. 21.
Differential Diagnosis of Chronic Extremity Symptoms. J. C. Luke.—p. 23.
Medical Shock and Death Following Neoarsphenamine Therapy for Syphilis. B. Kanee and G. R. F. Elliot.—p. 28.
Virus Infections of Central Nervous System. A. J. Rhodes.—p. 32.
Modern Approach to Psychoanalysis. N. Viner.—p. 36.
Vaginal Smear Technic for Diagnosis of Cancer in Female Genital Tract. J. D. Hamilton and M. O. Klotz.—p. 42.
Oral Administration of Penicillin. H. Starkey and J. H. Dixon.—p. 47.
*Sulpha Granuloma—New Pathologic Entity. T. H. Williams.—p. 50.
Results of Surgical Treatment of Coronary Artery Disease. C. B. Ripstein.—p. 52.
Ocular Manifestations of Myasthenia Gravis. B. Teichman and K. C. Greer.—p. 55.
Assessment of Results of Vagotomy: Based upon Personal Experience of 66 Cases. L. H. Appleby.—p. 58.

Five Week Penicillin-Oxophenarsine-Bismuth Schedule in Early Syphilis.—The treatment described by Marin and his co-workers consists in the administration of penicillin, oxophenarsine hydrochloride and bismuth compound over a period of five weeks, necessitating hospitalization for the first week. During the first week, the three drugs are given simultaneously. During the four following weeks only oxophenarsine and bismuth compound are given. Sodium penicillin in aqueous solution is administered intramuscularly every three hours, in sixty injections of 40,000 units each. A total dose of 2,400,000 units is thus received in seven and one-half days. Oxophenarsine is given at the rate of four injections of 60 mg. each, every week, for five weeks, the total dose being 1,200 mg. in twenty injections. Bismuth compound, in oil solution, containing 0.07 Gm. of metallic bismuth per cubic centimeter, is administered at the rate of 1 cc. twice a week for five weeks. In May 1945, this schedule of treatment was adopted for cases of early syphilis. Up to November 1947, 230 patients were placed under treatment. Of these, 222 received complete treatment. A total of 201 cases have been kept for final analysis. The 29 others were eliminated because of previous treatment, late syphilis, doubtful diagnosis or delinquency from treatment. There was one fatality due to encephalopathy (0.4 per cent); there were no other severe toxic reactions. Satisfactory progress was obtained in 100 per cent of 36 cases of seronegative primary syphilis, in 90 per cent of 55 cases of seropositive primary syphilis and in 86 per cent of 94 cases of secondary syphilis. The over-all results show 90 per cent satisfactory progress and 4.5 per cent definite treatment failures, with the other 6 per cent pending.

Rutin in Hematuria.—Foucar reports a woman, aged 44, with bilateral congenital polycystic kidneys, gross hematuria, definite impairment of renal function, hypertension and mild secondary anemia. As nothing could be done to improve the underlying lesion, the author decided to try rutin. Twenty milligrams of rutin to which 50 mg. of ascorbic acid had been added was given three times a day with gratifying results. The bleeding stopped promptly. There has not been gross hematuria in six months. The patient feels better than at any time since 1945 and is working steadily. She is also relieved emotionally because of the supression of the visible signs of her disability. Rutin has been used in vascular disturbances particularly of the eyes and may lessen the danger of vascular accidents in hypertension. It may find a place in the treatment of shock, ascites, edema and even some of the eczemas.

Sulfonamide Granuloma.—Williams reports the case of a nurse who noted a tender swelling in her left breast. When application of heat and fomentation failed to resolve the swelling, the lesion was incised and a small bit of tissue removed. At this time sulfanilamide powder was dusted into the wound. Subsequently, the wound became tender and exuded a little serous discharge, healed and again broke down with a small sinus opening. The area was excised with the diagnosis of abscess of the breast. Tissue section showed chronic inflammatory reaction with numerous small areas of granuloma. Repeated subsequent sinus formation required additional incisions. Whereas granulomatous appearance was not found at the original examination of the tissue, such an appearance was found at all three specimens of tissue removed after sulfonamide powder was introduced into the tissues. Reviewing diagnoses for the past year, the author found a dozen reports of reamputations or reoperations in which pain and/or discharge from a surgical scar had been present. In all of the group definite crystalline inclusions were seen in foreign body giant cells. Records of the original operation usually indicated that sulfonamide powder had been dusted into the incision before closure. While the dusting of sulfonamide powder into the wounds at operation may not always produce granulomatous tissue reaction, it remains as unabsorbed foreign material in an appreciable number of cases and provokes a granulomatous tissue reaction.

Endocrinology, Springfield, Ill.

42:339-426 (May) 1948

Grafted Mouse Ovaries and Their Adrenal Cortical Function. R. T. Hill.—p. 339.
Cholesterol Studies of Adrenals and Plasma in Partially Hepatectomized and Partially Nephrectomized Rats After Injection of HNa. S. Ludewig and A. Chanutin.—p. 352.
Increased Protein Catabolism in Thyroidectomized Rats: Rates of Urine Urea Excretion and Serum Urea. E. C. Persike.—p. 356.
Increased Protein Catabolism in Thyroidectomized Rats: Anatomic Changes. E. C. Persike.—p. 363.
Response of Human Fetal Reproductive System to Administration of Diethylstilbestrol and Testosterone Propionate During Early Pregnancy. M. E. Davis and Edith L. Potter.—p. 370.
Assay of Adrenocorticotrophic Hormone by Adrenal Ascorbic Acid-Depletion Method. M. A. Sayers and L. A. Woodbury.—p. 379.
Lymphopenia Following Electrically Induced Convulsions in Male Psychotic Patients. W. P. Mikkelsen and T. T. Hutchens.—p. 394.
Effect of Inanition on Anterior Pituitary-Adrenocortical Interrelationship in Guinea Pig. S. A. D'Angelo, A. S. Gordon and H. A. Charipper.—p. 399.
Extra-Renal Action of Desoxycorticosterone: Survival and Water Intoxication Studies. J. H. Birnie, W. J. Eversole and R. Gaunt.—p. 412.

Iowa State Medical Society Journal, Des Moines

38:231-278 (June) 1948

Endometriosis. R. S. Cron.—p. 231.
Management of Peritoneal Soiling Complicating Surgery of Abdomen. M. J. Brown.—p. 234.
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Journal of Allergy, St. Louis

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Dissimilar Sensitivity to Antigen of Segments from Isolated Intestinal Strip. Alice H. Kempf and S. M. Feinberg.—p. 247.
Levels for Pyribenzamine and Benadryl in Blood and Urine Following Single Orally Administered Dose. T. H. McGavack and A. Heisler. —p. 251.
Studies on Histamine and Histamine Anatagonists. U. Serafini.—p. 256.
Antihistamine Drugs in Hay Fever: Comparative Study with Other Therapeutic Methods. W. I. Weiss and R. M. Howard.—p. 271.

Journal of Experimental Medicine, New York

88:1-148 (July) 1948

Cirrhosis and Other Hepatic Lesions Produced in Dogs by Thyroidectomy and by Combined Hypophysectomy and Thyroidectomy. I. I. Chaikoff, T. Hillman, C. Entenman and others.—p. 1.
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Phenomenon of in Vitro Hemolysis Produced by Rickettsiae of Typhus Fever, with Note on Mechanism of Rickettsial Toxicity in Mice. Delphine H. Clarke and J. P. Fox.—p. 25.
Immunochemical Studies on Blood Groups. E. A. Kabat, H. Baer, Ada E. Bezer and others.—p. 43.
Poliomyelitis in Cynomolgus Monkey: Further Observations on Exposures Confined to Stomach and Intestines, with Notes on Fecal Excretion of Virus. H. K. Faber, Rosalie J. Silverberg and L. Dong. —p. 65.
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Journal of International College of Surgeons, Chicago

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*Radicability of Methods to Eliminate Colostomy: Critical Review. H. E. Bacon and R. J. Rowe.—p. 243.
Treatment of Metastatic Cancer in Cervical Lymph Nodes. J. V. Blady. —p. 253.
*Nonfunctioning Gallbladder. W. Bates and G. King.—p. 265.
New Method of Esophagoplasty. G. M. Mes.—p. 270.
Experimental and Clinical Observations on Hypothermia and Procaine. F. M. Allen.—p. 278.
Cutis: Its Various Uses in Surgery. J. E. Cannaday.—p. 282.
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Resection of Rectosigmoid Region with Preservation of Anal Sphincter. C. S. White.—p. 303.
Aseptic Necrosis of Bone Following Trauma. E. L. Compere.—p. 310.
Ten Years of Plastic Surgery in Penal Institution: Preliminary Report. J. F. Pick.—p. 315.
Present Status of Treatment of Varices and Their Complications. C. A. Protzel and P. Icochea.—p. 325.

Radicalness of Methods to Eliminate Colostomy.—Bacon and Rowe performed abdominoperineal proctosigmoidectomy for adenocarcinoma in 146 patients, 78 men and 68 women, between the ages of 32 and 78 years. The extirpated specimen of bowel was sectioned 2, 4 and 6 cm. below the lower edge of the growth. An abdominoperineal proctosigmoidectomy without colostomy was performed in all. This operation was instituted only when the distance between the anal margin and the lower border of the growth was 6 cm. or more. Preservation of the sphincter musculature does not compromise radicalness provided specific principles are carefully adhered to. The radicalness of proctosigmoidectomy compares favorably with other procedures, and in some respects it permits of even wider excision. The survival rate of five and ten year cures is equal to and in some instances betters the results following the abdominoperineal excision of Miles or the perineoabdominal excision of Gabriel. This is true especially when the rate of resectability is considered. Of the 77 patients resected more than five years ago 41 (52.6 per cent) are living and well. In 20 of these 77 patients the histopathologic reports conformed to grade A growth, with 14 of them alive at five years. Proctosigmoidectomy with preservation of the sphincter musculature does not augment the operative mortality; 18 of 376 patients on whom this operation was performed by the authors for cancer died, a mortality rate of 4.9 per cent. The morbidity, immediate and remote, is in no way affected. A consecutive group of 120 patients, 70 men and 50 women, between the ages of 29 and 73, is reported in which the average stay in bed was 6.6 days and the average hospital stay after operation was 13.4 days.

Nonfunctioning Gallbladder.—Bates and King studied 200 patients with chronic cholecystitis who had been subjected to surgical treatment. There were 18 in whom the gallbladder had been poorly or not all visualized and in whom there were no opacities suggesting gallstones roentgenographically. The general incidence of nonfunctional or nonfilling gallbladder was 9 per cent. There were 4 men and 14 women. The average age was 51 years, with about equal distribution in each decade from 30 to 70 years of age. In no case in this series did intravenous administration of the dye give visualization of the gallbladder if visualization had not been obtained after "intensified oral administration" of the dye. A competent radiologist's report of a nonfunctioning or nonfilling gallbladder carries with it the implication of advanced pathologic change, increased morbidity, difficult surgery and increased mortality. Advanced pathologic change was demonstrated at operation in all cases of nonfunctioning gallbladder in this series. Three of the 18 patients died; since there were only 6 deaths in the entire series of 200 patients, deaths in the nonfunctioning group contributed 50 per cent of the over-all mortality rate. The follow-up records of all 15 surviving patients indicate that good results after leaving the hospital may be expected with surgical treatment of the nonfunctioning gallbladder.

Journal of Investigative Dermatology, Baltimore

10:397-470 (June) 1948

Specificity of Streptococci Isolated from Patients with Skin Disease (Studies on Pemphigus, Dermatitis Herpetiformis, Lupus Erythematosus and Erythema Multiforme): IV. Erythema Multiforme. A. L. Welsh.—p. 401.
Immediate Urticarial Reaction to Intradermal Testing in Penicillin Hypersensitivity. J. Farrington and J. Tamura.—p. 421.
Present Status of Passive Transfer Antibodies in Allergic Eczematous Contact-Type Dermatitis: Failure to Demonstrate Passive Transfer Antibodies. M. Leider and R. L. Baer.—p. 425.
Leishmania Test in Experimental Leishmaniasis (Oriental Sore) in Human Subjects. A. Dostrovsky.—p. 435.
*Bistrimate for Lupus Erythematosus, Lichen Planus and Other Dermatoses. Frances Pascher, H. H. Sawicky, Mabel G. Silverberg and R. Emmet.—p. 441.
Copper Undecylenate in Treatment of Dermatomycoses. F. C. Combes, Ruth Zuckerman and A. Bobroff.—p. 447.
Treatment of Psoriasis with Liquor Carbonis Detergens: Modifications of Goeckerman Treatment. C. C. Ellis, W. E. Wooldridge and R. S. Weiss.—p. 455.

Sodium Bismuth Triglycollamate for Dermatoses.—Pascher and her associates studied the therapeutic effects of "bistrimate" (sodium bismuth triglycollamate) in 92 patients with various dermatoses. There were 45 patients with lupus erythematosus, 32 with lichen planus; the other dermatoses included granuloma annulare, psoriasis, scleroderma and other disorders. The therapeutic assay indicates that the drug is a valuable agent in the treatment of the discoid type of lupus erythematosus. The results in this disease may be rated as good to excellent in 50 per cent of the cases, moderate or fair in 25 per cent and poor in 25 per cent. It is more difficult to evaluate the efficacy of the drug in the exanthematic type of lichen planus, particularly because of the variable course of this disease. Subjective or objective improvement was obtained in 40 per cent of the cases. Twelve per cent grew worse or suffered relapse while under treatment. The results are also equivocal in the hypertrophic form of licen planus. The results in the limited number of cases of scleroderma and granuloma annulare allow no inferences but appear to justify further therapeutic investigation. In general the drug is tolerated well. Recovery from the apparently mild toxic effects was complete within a few days to two weeks in all cases in which sodium bismuth triglycollamate had to be discontinued because of untoward reactions.

Journal of Neurophysiology, Springfield, Ill.

11:279-398 (July) 1948. **Partial Index**

Effect of Delay of Innervation on Recovery of Muscle After Nerve Lesions. E. Gutmann.—p. 279.
Response of Single Ranvier Nodes to Electrical Stimuli. I. Tasaki and K. Mizuguchi.—p. 295.
Action Currents of Single Nerve Fibers as Modified by Temperature Changes. I. Tasaki and M. Fujita.—p. 311.
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Effect of Potassium on "Resting" Potential and Respiration of Crab Nerve. A. M. Shanes and H. S. Hopkins.—p. 331.
Analysis of Synaptic Excitatory Action. C. McC. Brooks and J. C. Eccles.—p. 365.
Antidromic Potential Recordings from Bulbar Pyramid of Cat. J. M. Brookhart and R. E. Morris.—p. 387.

Journal of Urology, Baltimore

60:1-196 (July) 1948. **Partial Index**

Incidence and Extent of Hydronephrosis in Prostatic Obstruction. H. L. Kretschmer and F. H. Squire.—p. 1.
Osteogenic Sarcoma Involving Right Kidney. H. G. Hamer and W. N. Wishard.—p. 10.
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Megalo-Ureter. E. W. Campbell.—p. 31.
Diagnosis and Management of Ureteral Ectopia. T. D. Moore.—p. 50.
Injury of Ureter Due to Gunshot Wounds. C. F. Rusche.—p. 63.
Reimplantation of Skin Ureterostomies into Bowel. S. A. Beisler.—p. 76.
Remote End Results of Management of Pedunculated Bladder Tumors. E. G. Crabtree.—p. 85.
Treatment of Bladder Tumors. A. L. Dean.—p. 92.
*Total Cystectomy in Treatment of Vesical Carcinoma. D. O. Ferris and J. T. Priestley.—p. 98.
*Infiltrating Carcinoma of Bladder: Curability by Total Cystectomy. H. J. Jewett and E. L. Lewis.—p. 107.
Hemolysis During Transurethral Prostatic Resection. R. G. Bunge and A. P. Barer.—p. 122.
One-Stage Suprapubic Prostatectomy with Primary Closure of Bladder. W. C. Eikner.—p. 124.
Suprapubic Prostatectomy, Restatement of Principles. A. L. Stockwell.—p. 128.
Pathology of Mumps Orchitis. C. W. Charny and D. R. Meranze.—p. 140.
Lipoma of Scrotum: Case Report. G. R. Livermore.—p. 153.
Congenital Male Sterility. A. Trabucco.—p. 156.
Male Sterility (Or Impaired Fertility). E. A. Slotkin.—p. 166.
Results of Clinical Study in Use of Streptomycin in Urinary Infections. F. K. Garvey and T. E. Canning.—p. 176.
Use of Streptomycin in Treatment of Tuberculosis of Urinary Tract. E. N. Cook and L. F. Greene.—p. 187.

Total Cystectomy in Vesical Carcinoma.—Ferris and Priestley list the following indications for cystectomy, with the reservation that they constitute merely a working plan on which they have been selecting patients: (1) a low grade lesion with minimal or moderate infiltration, provided it involves a major portion of the vesical wall; (2) a similar type of lesion which is of multicentric origin; (3) repeatedly recurring lesions of low grade; (4) an infiltrating or high grade lesion which cannot be widely removed by segmental resection, and (5) any vesical carcinoma the complete removal or destruction of which would result in serious interference with normal vesical function. Recurrent high grade lesions seldom are suitable for radical surgical treatment because of extravesical extension. Different procedures are employed currently to accomplish removal of the bladder. At the Mayo Clinic, cutaneous ureterostomy has been performed in only 7 per cent of the 111 cases in which total cystectomy has been accomplished for carcinoma in the ten years 1937 to 1946, inclusive. For the most part, procedures other than ureterosigmoidostomy were employed in the earlier cases and have been used less frequently during recent years. It is undesirable to transplant one ureter to the skin and the other to the bowel, as the patient then has the disadvantages of both these abnormal methods of urinary drainage. The authors started to use three stages, transplanting each ureter to the bowel in separate stages and subsequently removing the bladder. Later, 2 stages were employed, a simultaneous bilateral ureterosigmoidostomy constituting the first stage and removal of the bladder forming the second stage. During the past 3 years, 1 stage has been used in the majority of the cases. Thus, in 1946, total cystectomy was performed in 33 cases and in 24 cases a one stage operation was employed. The 1 stage procedure now is the method of choice, but it should not be suggested until familiarity with the operation has been acquired. The hospital mortality rate for 1942 to 1946, inclusive, was 8 per cent, as compared with a rate of 25 per cent for the previous five years, 1937 to 1941, inclusive. The ultimate results depend, to a great extent, on the type of case in which this operation is performed. Whereas 29 per cent of patients survived three or more years after operation, only 19 per cent survived five or more years after cystectomy.

Cystectomy for Infiltrating Carcinoma of Bladder.—Jewett and Lewis discuss the correlation between the exact depth to which the tumor has penetrated the vesical wall and the survival of the patient after cystectomy. Their studies were made on 54 patients. In 41 cases in which the infiltration was deep there were no instances of cure. In 13 cases in which the infiltration was superficial there were only 2 patients who were known to have died of cancer. Three patients have lived over five years without evidence of recurrence of tumor. A preoperative pelvic examination was made and the results recorded in 40 of these 54 cases of cystectomy. In each of 31 cases in which deep infiltration was found microscopically, it had been detected before operation by palpation of a rubbery or stony hard mass in the vesical wall. When rubbery or stony induration was absent on preoperative examination, subsequent microscopic sections always showed superficial infiltration. The over-all end results of total cystectomy cannot be compared with those obtained by conservative procedure, since the conservative methods are often employed in the cases of smaller tumors which are apt to be potentially curable, whereas cystectomy in the past has been reserved for the most part as a heroic measure in deeply infiltrating, extensive and incurable tumors.

Kansas Medical Society Journal, Topeka

49:229-276 (June) 1948

Treatment of Congestive Heart Failure. A. C. Ernstene.—p. 229.
Periarteritis Nodosa: Report of Case with Unusual Features. N. Uhr and R. Chess.—p. 232.
Problems of Anesthesia for Tuberculous Patient. Gretchen Guernsey and P. H. Lorhan.—p. 238.
Psychiatric Program of University of Kansas Medical Center. W. F. Roth Jr.—p. 241.

49:277-320 (July) 1948

Choice of Anesthetic Agents and Procedures. E. B. Tuohy, T. A. Guenther and F. J. Grabill.—p. 277.
Indications and Contraindications for Splenectomy in Hematologic Diseases. S. J. Wilson.—p. 281.
Rh Negative Mother in Private Obstetric Practice. R. A. West and N. C. Siebert.—p. 285.
*Use of Testosterone Propionate in Nitrogen Retention. F. W. Matassarin.—p. 287.

Testosterone Propionate in Nitrogen Retention.—Matassarin noticed that when testosterone was used in the treatment of patients with prostatic disorders the nonprotein nitrogen returned to normal more quickly than would have been expected with catheter drainage alone. He used this hormone in 50 cases with reduction of the urea nitrogen. These cases have included both men and women, ranging in ages from 21 to 83 years. They cover a variety of conditions, such as nephritis, prostatis, cholecystitis, heart disease, prostatic hypertrophy, toxemia of pregnancy, postoperative intestinal obstruction and senility. The author hopes that others will study this problem further, both clinically and experimentally.

Kentucky Medical Journal, Bowling Green

46:253-300 (July) 1948

Vascular Degeneration. E. L. Bortz.—p. 257.
Treatment of Syphilis. G. Brockman.—p. 263.
Management of Occipito Posterior Positions. C. J. McDevitt.—p. 269.
Résumé of Treatment of Acute Sinusitis. J. S. Bumgardner.—p. 271.
Recent Advances in Treatment of Pulmonary Tuberculosis. J. S. Harter.—p. 273.
Boecks Sarcoidosis. O. O. Miller.—p. 277.
Tumors of Kidney: Classification and General Conditions. J. A. Bowen—p. 282.
Clinical Manifestations of Renal Neoplasm. J. M. Townsend.—p. 283.
Therapy from Standpoint of Surgery and Radiation. L. Atherton.—p. 285.
Eye Manifestations of Vascular Systemic Disturbances. D. J. Lyle.—p. 287.
Use of Rabbit Serum in Treatment and Prophylaxis of Whooping Cough. M. Z. Kaplan and J. B. Larson.—p. 292.

Michigan State Medical Society Journal, Lansing

47:690-816 (July) 1948

Newer Concepts in Diagnosis of Glaucomas. H. S. Sugar.—p. 721.
Osteochondritis Dissecans and Osteochondromatosis. L. L. Swenson.—p. 728.
*Benign Pulmonary Histoplasmosis: Familial Incidence. R. F. Weyher.—p. 737.
Aims and Purposes of the Specialty Boards: Special Reference to the American Board of Surgery. J. S. Rodman.—p. 741.
The Nursing Problem. T. P. Murdock.—p. 745.
Nursing—Service Aspects. Janet M. Geister.—p. 747.

Benign Pulmonary Histoplasmosis: Familial Incidence.—Weyher points out that whereas earlier reports were concerned with the form which has a grave prognosis, recent reports indicate that there is a benign pulmonary form of histoplasmosis, which is widespread throughout some sections of the United States. The author reports a family group, parents and 3 children, who have lived intermittently in Tennessee. Four of the group are considered to have benign pulmonary histoplasmosis. Although the entire family has been observed for nearly three years, and all members are clinically well at the time of this report, serial roentgenograms of 2 of the children, showing widespread pulmonary calcifications, demonstrate increasing density of the individual areas involved during the period of study. The reactions to histoplasmin in this family and the reproduction of Histoplasma capsulatum are not to be construed as proof of the causation of calcifications shown in the roentgenograms of the chest, since histoplasmin tests are not specific for this organism alone. Clinically the cases appear to fit descriptions of the benign form of this disease. Since no effective therapy exists for the disease, it is suggested that persons with so-called benign cases of the pulmonary form who move away from the areas in which they contracted the infection should avoid returning to the same regions for any protracted stay, especially during the summer months, since apparently reinfection may occur.

Nebraska State Medical Journal, Lincoln

33:225-260 (July) 1948

Abdominal Allergy. J. M. Sheldon.—p. 229.
Program for Improvement of Psychiatric Care in Nebraska. R. H. Young.—p. 232.
Immunization Against Influenza. W. Thompson.—p. 236.
Immunization Against Measles, Scarlet Fever. G. C. O'Neil.—p. 239.
Whooping Cough Immunization. H. M. Jahr.—p. 241.

33:261-296 (Aug.) 1948

Things I Want to Say. J. E. M. Thomson.—p. 264.
Prostatitis: Especially as It Relates to Cause, Treatment and Significance. R. B. Henline.—p. 266.
Convulsive Disorders: Modern Concepts—Diagnosis and Treatment. E. Kelley.—p. 274.
Symptomatic Seizures in General Medical Conditions. E. E. Simmons and R. S. Long.—p. 277.
Neurosurgical Aspects of Epilepsy. A. I. Finlayson.—p. 280.
Calcium, Phosphorus and Phosphate Metabolism. E. J. Kirk and D. R. Jackson.—p. 284.

New England Journal of Medicine, Boston

239:1-34 (July 1) 1948

Focal Epilepsy: Statistical Study of Its Causes and Results of Surgical Treatment. II. Epilepsy Secondary to Cerebral Trauma and Infection. J. C. White, C. T. Liu and W. J. Mixter.—p. 1.
Aggressive Behavior—Its Psychiatric and Physiologic Aspects, Especially in Combat Veterans. L. Alexander.—p. 10.
Primary Teratomatous Chorionepithelioma of Ovary: Report of Case. H. M. Oliver and E. O. Horne.—p. 14.
Yaws in Massachusetts. J. G. Downing.—p. 17.
Malaria. Q. M. Geiman.—p. 18.
Adenoacanthoma of Fundus of Uterus.—p. 23.
Malignant Lymphoma, Hodgkin's Type.—p. 25.

239:35-74 (July 8) 1948

Retropubic Prostatectomy. G. Austen Jr. and W. C. Quinby.—p. 35.
Amebic Abscess of Liver. Therapeutic Problems in Various Types of Late Hepatic Amebiasis. E. H. Drake and T. A. Warthin.—p. 45.
*Desirability of Routine Use of Tetanus Toxoid. E. Press.—p. 50.
Papillary Cystadenocarcinoma of Both Ovaries: Report of Case with Apparent Cure Eight Years After Operation. G. L. Gaudrault.—p. 56.
Malaria. W. M. Geiman.—p. 58.
Papillary Serous Adenocarcinoma.—p. 64.
Tuberculous Salpingitis and Endometritis.—p. 67.

Desirability of Routine Use of Tetanus Toxoid.—According to Press, additional information regarding the effectiveness and hazards of active immunization against tetanus has become available during the last few years. Press presents evidence for and against routine active immunization. It was found that about 50 per cent of all injuries leading to tetanus in the civilian population were trivial. The majority of bacteriologic studies revealed that tetanus spores were widely distributed and more frequently found in human feces than in those of horses. The mere presence of tetanus spores in a wound was not sufficient to cause the disease. Statistical evidence shows that less than 20 per cent of the cases of tetanus are reported in the United States. There were at least 910 deaths due to tetanus in the United States in 1940. The conscientious physician, aware of the widespread distribution of tetanus spores, knowing the potentiality of tetanus with trivial injuries and being unable to determine which cases might go on to develop it, would be forced to give tetanus antitoxin for nearly all injuries. In view of the definite effectiveness of tetanus toxoid and its almost complete freedom from adverse reactions, its use seems to be indicated. The not infrequent failure of tetanus antitoxin prophylactically is indicated by the fact that in spite of its use tetanus developed in about 7 per cent of civilian and over 50 per cent of military cases. To avoid the increased risk of anaphylaxis and the more frequent allergic reactions to repeated doses of tetanus antitoxin, it is advisable to give toxoid concurrently with each inoculation of tetanus antitoxin. If this active immunization is then completed, it should be unnecessary to use antitoxin for any future injuries in a person by then sensitized to horse serum. Active immunization against tetanus is indicated. It should be given routinely by private physicians and should also be included in health department programs for all children. The toxoid should be given to children combined with diphtheria or pertussis vaccine, or both. In addition, children who have been immunized for diphtheria and pertussis, but not for tetanus, should have tetanus toxoid available and be encouraged to use it. Adults with increased accident hazards, such as manual laborers in both rural and urban areas, should also be immunized.

New Orleans Medical and Surgical Journal

100:445-490 (April) 1948

Pruritus Ani and Vulvae. M. T. Van Studdiford and L. D. McLean.—p. 445.
Present Status of Knowledge Concerning Spread of Poliomyelitis. D. E. Loveman.—p. 449.
Urologic Complication Following Operation for Imperforate Anus. R. F. Sharp and A. Brin.—p. 456.
Central Fractures of Neck of Femur: Critical Review of 300 Cases. I. L. Geroge.—p. 459.
Double Notched Graft for Lumbosacral Spine Fusion. A. R. Altenberg.—p. 464.
Congenital Ocular Anomalies Resulting from (a) Premature Birth (b) Rubella Infection of Mother During Pregnancy. W. R. Buffington.—p. 466.
*Intravenous Ether (Diethyloxide): Use in Treatment of Cases of Impending Gangrene and Impaired Circulation. O. C. Williams.—p. 470.
Fractured Ribs from Coughing. J. M. Bodenheimer.—p. 474.
*Sulfone Treatment of Leprosy. P. T. Erickson, R. R. Wolcott and F. A. Johansen.—p. 475.

Intravenous Ether in Impending Gangrene.—Williams reports on the intravenous use of ether in the treatment of 22 patients with impending ischemic gangrene, diabetic ischemia, arteriosclerosis and hypoplastic ulcer. He used a 2.5 per cent solution of ether—namely, 25 cc. of stock ether to 1,000 cc. of 5 per cent dextrose in distilled water or in isotonic sodium chloride solution—in all of his cases. The 1,025 cc. of solution is given daily, intravenously, the flow being started at 40 drops per minute, and if no reaction occurs, being stepped up to about 50 drops per minute, but not over 60 per minute. He decided that twelve bottles would represent a course, and that he would then give a few days rest, and repeat all laboratory tests before starting on a second course. All patients were thoroughly studied prior to treatment. Blood pressure reading, pulse and temperature records were made during the administration of the drug. Results have been encouraging. Relief from pain has been one of the most gratifying findings. The treatment with ether has not been unpleasant to the patient. It is considered a safe drug in the given dilution. It can be given while the patient is being prepared for operation.

Sulfone Treatment of Leprosy.—Erickson and his associates say that the sulfone drugs have proved to be more effective in lepromatous leprosy than any previous drug tried at Carville. "Promin" (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate), "diasone" (disodium formaldehyde

sulfoxylate diaminodiphenylsulfone) and "promizole" (4,2'-diaminophenyl-5'-thiazolylsulfone) are related chemically to one another by having in common the diaminodiphenylsulfone radical. There is reason to believe that the diaminodiphenylsulfone radical is the active principle, although this has not been definitely established. No claim is made that these drugs are specific remedies for leprosy, but the superiority of the sulfones over chaulmoogra oil is significantly demonstrated by the complete abandonment of the latter treatment in favor of the sulfones at Carville. Objective and subjective clinical improvements are produced by these drugs that cannot be attributed to spontaneous regression of the disease. Improvements are slow in their development but are progressive during treatment. The disease seldom if ever gets worse during treatment. Laboratory examinations indicate a slow but steady decrease in acid-fast organisms in the skin. Negative cutaneous smears and arrest of the disease occur. So far no relapse in arrested cases has been reported.

New York State Journal of Medicine, New York

48:1423-1534 (July 1) 1948

Estrogens in Diabetes. H. Marcus and S. Glotzer.—p. 1461.
Use of New Antihistaminic Combination in Treatment of Allergic Disorders. E. B. Brown and F. W. Brown.—p. 1465.
Devices for Rapid Recording of Unipolar Electrocardiogram. A. Lieberson and A. A. Goldbloom.—p. 1467.
Streptomycin and Surgery in Treatment of Tuberculous Joints. A. A. Michele and F. J. Krueger.—p. 1470.
Clinical Evaluation of Neo-Antergan and Antistine in Treatment of Ragweed Hay Fever. L. Levin and E. Schwartz.—p. 1474.
Streptomycin in Chronic Tuberculosis. J. N. Hayes and H. F. Parry.—p. 1477.
*Gangrene of Both Legs Following Femoral Vein Ligation. J. Sarnoff.—p. 1480.
Treatment of Venous Thrombo-Embolism. S. W. Cospriff, R. J. Cross and D. V. Habif.—p. 1483.
What Is Normal Blood Pressure? H. I. Russek.—p. 1485.
Surgical Treatment of Hypertension. D. P. Boyd.—p. 1487.
Electrocardiogram in Catatonic Schizophrenia. S. Major.—p. 1489.
Pilonidal Cyst Surgery: Modification. A. J. Cantor.—p. 1492.
Management of Severe Postlumbar Puncture Headache. R. E. Ahearn.—p. 1495.

Gangrene of Legs Following Ligation of Femoral Vein.—Sarnoff reports the case of a man, aged 50, who suffered a heart attack in December 1946 for which he was hospitalized for four weeks. When he was almost well enough to go home he had two attacks of chills. To avoid the possibility of emboli, the attending physician advised ligation of both femoral veins, which was done the following day. Immediately after the ligation both legs became cyanotic, and in the course of the next few days became gangrenous. The patient received a number of paravertebral nerve blocks in the hope of relieving the spasm of the arteries, and thereby helping to establish collateral circulation, but to no avail. Both legs were amputated below the knee. Similar accidents have occurred. They illustrate that ligation of the femoral vein is not to be considered lightly.

Ohio State Medical Assn. Journal, Columbus

44:671-768 (July) 1948

Collateral Findings and Supportive Therapy in Acne Vulgaris. J. D. Walters.—p. 697.
*Non-Tuberculous Pulmonary Calcification. J. A. Prior.—p. 700.
Some Further Observations on Prognosis After Coronary Occlusion. H. C. King.—p. 704.
Palindromic Rheumatism—Effective Treatment with Gold. M. Ginsburg.—p. 707.
*Complete Transposition of Great Cardiac Vessels. E. W. Miskall and J. A. Fraser.—p. 709.
Cosmetic Plastic Surgery—Its Relationship to Personality. J. G. Himmel.—p. 711.
Hydatidiform Mole in a Twin Pregnancy with Viable Fetus. H. V. Mishler and G. R. Dickerhoof.—p. 714.
Psychiatric Units in General Hospitals. L. Pillersdorf.—p. 716.
Myxedema Heart with Cardiac Failure. R. H. Schoene and A. L. Pollock.—p. 718.
Fibroma of Ovary with Ascites and Hydrothorax. P. M. Spurney.—p. 722.

Nontuberculous Pulmonary Calcification.—Prior says that in recent years the possible relationship between calcified lesions of the lungs, especially as they occur in the Eastern Central states, and the rare fungus disease histoplasmosis has been a subject of growing interest. Studies in Ohio have confirmed in general this geographic pattern of the incidence of positive histoplasmin reactors. Five thousand and eighty-seven Ohio State University freshmen and student nurses training in Columbus, all of whom were lifetime residents of some one county, were surveyed with roentgenograms of the chest, tuberculin and histoplasmin cutaneous tests. Every county in the state was represented in the group studied. The author believes that in the Eastern Central portion of the United States there is a better correlation between pulmonary calcifications and a positive histoplasmin reaction than with a positive intradermal tuberculin reaction, and in cases of disseminated pulmonary calcification there is an even higher incidence of histoplasmin reactors. This same geographic area in which there is excessive pulmonary calcification with not infrequent miliary distribution corresponds rather closely to both the endemic area of histoplasmosis and the region of high incidence of histoplasmin reactors. The concept of the causation of pulmonary calcifications needs revision. Although many are the result of a true tuberculous infection, calcification may also occur as the result of benign forms of coccidioidomycosis and histoplasmosis or other closely related agent or agents with similar antigenicity.

Transposition of Great Cardiac Vessels.—Miskall and Fraser report the case of a white infant girl with a bifid eighth thoracic vertebra and other defects, who died in the eleventh month. This case typifies one of those cyanotic congenital cardiac defects for which, according to Blalock and Taussig, surgical treatment is of no value. In this anomaly there is an altered relationship of the great vessels to one another and to their respective ventricles in such a manner that the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. The blood is pumped from the left ventricle through the pulmonary artery to the lungs, and it returns to the left auricle through the pulmonary veins. Through the aorta the blood is pumped by the right ventricle to the greater systemic circuit. It returns to the right side of the heart through the venae cavae. In the absence of a septal defect, this condition is incompatible with life since no oxygenated blood can go from the pulmonary to the systemic circulation.

Philippine Medical Association Journal, Manila

24:281-350 (June) 1948

Role of Philippine Medical Association in Promotion of Public Health. G. Rustia.—p. 293.
For Medical Service Within Reach of Poor People. F. Lopez.—p. 307.
Extensive Bone Formation in Vitreous Chamber in Atrophic Eyeball: Report of Case. A. S. Fernando and F. T. Bongco.—p. 313.
Five Unusual Surgical Diseases of Abdomen. F. C. Guzman and R. L. Alfonso.—p. 317.
Relation of Tropical Diseases to Surgery. P. M. Recio.—p. 323.
Biochemical Studies on Tuberculosis: II. Nucleic Acid Reaction of Serum in Tuberculosis. J. F. Leyva.—p. 327.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

68:1-224 (May) 1948. **Partial Index**

*Differential Agglutination of Normal and Sensitized Sheep Erythrocytes by Serums of Patients with Rheumatoid Arthritis. H. M. Rose, C. Ragen, Elizabeth Pearce and Miriam O. Lipman.—p. 1.
Chloromycetin in Treatment of Patients with Typhus Fever. J. E. Smadel, A. P. Leon, H. L. Ley Jr. and G. Varela—p. 12.
Outbreak of Equine Encephalomyelitis, Eastern Type, in Southwestern Louisiana. B. F. Howitt, L. K. Bishop, R. H. Gorrie, R. E. Kissling and others.—p. 70.
Penicillin in Cerebrospinal Fluid Following Parenteral Penicillin. W. P. Boger, R. B. Baker and W. W. Wilson.—p. 101.
Lipid Anticoagulant from Brain Tissue: Physiochemical Characteristics and Action in Vitro and in Vivo. L. M. Tocantins, R. T. Carroll and T. J. McBride.—p. 110.
Isolation of Vitamin K_2 from Cultures of Spore-Forming Soil Bacillus. M. Tishler and W. L. Sampson.—p. 136.
Changes in Electrocardiogram Associated with Standing. D. Scherf and M. Schlachman.—p. 150.
Effect of Phrenicotomy on Gastrointestinal Mechanisms. N. C. Jefferson and H. Necheles.—p. 166.
*Effect of Intravenous Administration of Human Serum Albumin on Renal Function. W. H. Cargill.—p. 189.
*Accidental Laboratory Infection with Human Dengue Virus. J. L. Melnick, E. C. Curnen and A. B. Sabin.—p. 198.

Agglutination of Sheep Erythrocytes by Serum of Patients with Rheumatic Arthritis.—Rose and his associates describe a differential sheep cell agglutination test wherein the agglutination titers of human serum for normal and sensitized sheep erythrocytes are compared. High differential titers have been found to occur almost solely in the serums of patients with active rheumatoid arthritis. Although the nature of the

substance and its significance with regard to the rheumatoid state remain to be determined, the present observations indicate that the sheep cell differential agglutination test may be of value in determining the activity status of patients suffering from rheumatoid arthritis. It may also prove to be helpful in the differential diagnosis between rheumatoid arthritis and other diseases with arthritic manifestations, such as rheumatic fever.

Administration of Serum Albumin and Renal Function.—Cargill points out that Thorn and co-workers had noted that the intravenous infusion of concentrated human serum albumin often produces a transient diuresis in patients with nephrosis and Laennec's cirrhosis. These authors studied the immediate effect of rapid injection of a large amount of albumin on glomerular filtration rate and renal blood flow. The clearance technics of Smith, Goldring and Chasis have been followed, using inulin and sodium para-aminohippurate. Rapid intravenous infusion of 75 Gm. of human serum albumin produced a consistant increase in glomerular filtration rate and renal blood flow. These changes were accompanied by both an increased clearance and a decreased tubular extraction of sodium para-aminohippurate. In 2 patients with nephrotic syndrome of chronic glomerulonephritis administration of albumin increased the filtration rate from low to normal levels, and in 1 of these patients it produced considerable diuresis.

Laboratory Infection with Dengue Virus.—Melnick and his co-workers say that in the course of experiments with chimpanzees, human dengue virus was accidentally introduced onto the conjunctival surface of the eye of a laboratory worker. This was followed nine days later by a febrile illness, clinically compatible with dengue. Neutralizing antibodies for the homologous mouse-adapted strain of dengue virus were absent in the patient's serum taken one day after the onset of fever, but were present in high titer in specimens of serum obtained thirteen, twenty-five and forty-five days after onset.

Psychoanalytic Quarterly, Albany, N. Y.

17:149-302 (April) 1948

Three Tributaries to Development of Ambivalence. E. Bergler.—p. 173.
Concurrent Analysis of Married Couples. B. Mittelmann.—p. 182.
Problems of Psychoanalytic Training. M. Gitelson.—p. 198.
Boswell: The Biographer's Character. Psychoanalytic Interpretation. E. Hitschmann.—p. 212.
Effects of Shock Treatment on Ego. J. Frosch and D. Impastato. —p. 226.
Dynamic Basis of Anti-Semitic Attitudes. N. W. Ackerman and Marie Jahoda.—p. 240.

Psychosomatic Medicine, Baltimore

10:133-192 (May-June) 1948

Infantile Personality: Core Problem of Psychosomatic Medicine. J. Ruesch.—p. 134.
Effect of Anxiety on Human After-Discharges: Psychosomatic Study of After-Contraction. M. R. Sapirstein.—p. 145.
Personality Types in Soldiers with Chronic Nonulcer Dyspepsia. S. R. Rosen, Helen Keosian, R. Schwartz and others.—p. 156.
Experiment with Comprehensive Medicine. G. Saslow.—p. 165.

Radiology, Syracuse, N. Y.

50:725-882 (June) 1948

Some Considerations of Roentgen Diagnosis of Silicosis and Conditions That May Simulate It. E. P. Pendergrass and A. G. Robert.—p. 725.
Significance of Occupational History in Diagnosis of Silicosis. T. F. Hatch.—p. 746.
Anthraco-Silicosis. W. J. Corcoran.—p. 751.
Pathogenesis of Industrial Pulmonary Disease. W. Machle.—p. 755.
Further Observations of Lung Changes Associated with Manufacture of Alumina Abrasives. C. G. Shaver.—p. 760.
*Delayed Chemical Pneumonitis or Diffuse Granulomatosis of Lung Due to Beryllium. S. A. Wilson.—p. 770.
Penile Carcinoma: Review of 43 Cases Treated at Bellevue Hospital During Past Twenty-Five Years. J. Zausner.—p. 786.
Studies of Circulation by Roentgencinematography. N. Westermark. —p. 791.
Preliminary Observations on Effects of Irradiation upon Chylomicrons in Human Blood. Kai Setälä.—p. 803.
Effects of Small Daily Doses of Fast Neutrons on Mice. T. C. Evans. —p. 811.

Chemical Pneumonitis Due to Beryllium.—Wilson shows that opportunity for exposure to beryllium starts in the beryl mines. In plants engaged in extracting beryllium from the ore and in the production of beryllium salts and oxides there has been definite evidence of disease among employees. The same has been true in metallurgical plants where beryllium has been used as a constituent in the production of alloys. Cases have been reported in workers coating fluorescent lamps and neon tubes. At least 1 case has arisen in the radio tube industry, and a few where the metal or its oxide was being ground. Beryllium or its compounds may be found in chemical and pharmaceutic plants. It is a possible hazard in research laboratories. Its use has been reported where gas mantles and some ceramics are made. Not all of these industries have experienced the development of pulmonary disease among their workers. In those that have, the symptoms, roentgen pattern and pathologic changes have been so similar that a common denominator is suspected, this denominator being beryllium or one of its compounds. The recognition of the roentgen manifestations of the pulmonary changes in beryllium workers is most important.

South Dakota Journal of Medicine, Sioux Falls

1:179-216 (May) 1948

Therapy of Common External Diseases of the Eye. E. P. Burch.—p. 179.
Climate and Resistance to Infection. C. A. Mills.—p. 184.
Porphyria (with Case Report). C. E. Kemper.—p. 187.
Transorbital Lobotomy: Preliminary Report of Twenty-Four Cases. F. W. Haas and D. B. Williams.—p. 191.
Streptomycin in Treatment of Complications of Whooping Cough. J. Decanie.—p. 193.

Southern Medical Journal, Birmingham, Ala.

41:575-666 (July) 1948. **Partial Index**

Reconstructive Surgery of Fallopian Tubes Employing Cannula. V. D'Ingianni.—p. 575.
Brain Repair: III. Some Practical Chronologic Aspects. S. P. Hicks. —p. 581.
Chronic Intestinal Intussusception in Adult. J. W. Snyder.—p. 586.
Management of Lye Burns of Esophagus. G. E. Fisher and J. J. Hicks. —p. 591.
*Anemia of Malignancy. A. J. Schwertman.—p. 598.
Practical Value of Liver Function Tests in Clinical Medicine. D. F. Marion and J. M. Rumball.—p. 601.
Untoward Reactions and Cutaneous Testing in Penicillin Therapy. J. Farrington, Kathleen Riley and S. Olansky.—p. 614.
Disappearing General Practitioner: Causes, Effects and Remedies. S. P. Kenyon.—p. 620.
Role of Small Community Hospital in Medical Education. W. T. Sanger.—p. 624.
Effectiveness of Various Diagnostic Criteria in Recognition of Subclinical Poliomyelitis in Field. A. E. Casey, W. I. Fishbein and I. Abrams.—p. 627.
Observations on Mood After Stellate Ganglionectomy. L. J. Karnosh and W. J. Gardner.—p. 631.
*Isopropyl Alcohol Intoxication. W. M. McCord, P. K. Switzer and H. H. Brill Jr.—p. 639.
Evaluation of Newer Therapy of Ulcerative Colitis. J. A. Bargen. —p. 646.

Anemia of Cancer.—The studies reported by Schwertman were made on 58 patients with carcinoma of eight common sites. They are based on the initial blood count, hemoglobin and color index. In 10 cases of carcinoma of the breast the average erythrocyte count was 4,300,000 and the color index was 0.98. The presence of metastases in these patients did not noticeably influence the concurrent anemia. In 10 cases of carcinoma of the colon, the average number of erythrocytes was 3,900,000, and the color index 0.9. In 10 cases of carcinoma of the prostate the average erythrocyte count was 4,390,000, and the color index 1.0. In 8 cases of carcinoma of the body of the uterus, the average erythrocyte count was 4,150,000 and the color index 0.92. In 4 cases of carcinoma of the bladder the respective figures were 4,110,000 and 0.95; in 7 cases of carcinoma of the cervix, 3,800,000 and 0.94; in 4 cases of carcinoma of the ovary, 4,001,000 and 0.95, and in 4 cases of carcinoma of the kidney, 4,500,000 and 0.98. In general, anemia is greater when hemorrhage, ulceration and necrosis occur. In some cases, even in the presence of metastasis, anemia does not occur.

Isopropyl Alcohol Intoxication.—McCord and his associates point out that as the industrial demand for ethyl alcohol has increased, isopropyl alcohol has been substituted for it wherever possible. Its use in industry is now widespread and it has become readily available to the general public in the form of rubbing alcohol. The authors present the histories of 3 patients who had ingested rubbing alcohol. In 2 of these isopropyl alcohol was chemically identified. In the third, there was a strong odor of isopropyl alcohol on the breath and in the stomach contents. The action of isopropyl alcohol on man is similar to the action of ethyl alcohol with the exception that

coma occurs at lower blood concentrations of isopropyl alcohol than of ethyl alcohol. In 2 cases a profound coma occurred with a blood concentration of isopropyl alcohol of approximately 150 mg. per hundred cubic centimeters. Treatment consisted of gastric lavage, fluids as indicated and symptomatic therapy. Recovery was rapid with no apparent untoward sequelae.

Surgery, St. Louis

24:1-160 (July) 1948

Resection of Thoracic Esophagus for Carcinoma Located Above Arch of Aorta: Cervical Esophagogastrostomy. J. H. Garlock.—p. 1.
Combined Left Abdominal and Right Thoracic Approach to Resection of Esophageal Neoplasms. J. E. Macmanus.—p. 9.
Intravenous Cholecystography with Tetraiodophthalic Fluorescein. G. E. Moore and M. J. Smith.—p. 17.
Method of Making Tubes of Polyethylene Film for Use in Anastomosis of Common Bile Duct, Trachea, and Pelvic Colon. J. H. Grindlay. —p. 22.
Management of Ileosigmoidal Fistula in Diverticulitis: Clinical Syndrome and Report of 4 Cases. R. R. Best.—p. 30.
Tumors of Small Intestine. H. A. Weinberger and R. M. Paltauf. —p. 35.
Pancreatic Cyst: Internal Drainage Utilizing Roux Principle. A. V. Migliaccio and E. C. Laurelli.—p. 54.
Chronic Inflammatory Intestinal Obstruction Due to Enterobius Vermicularis. J. M. Miller and M. Ginsberg.—p. 57.
*Relation of Pancreatic Secretion to Peptic Ulcer Formation: Effect of Pancreatectomy, Ligation of Pancreatic Ducts, and Diabetes on Production of Histamine-Induced Ulcers in Dog. E. J. Poth, L. J. Manhoff Jr. and A. W. DeLoach.—p. 62.
Stomach as Cause of Difficulty in Intubating Human Duodenum with Introduction of Use of Gastric Balloon. J. J. Wild.—p. 70.
Experimental Studies in Vascular Repair: I. Comparison of Reliability of Various Methods of End-to-End Arterial Sutures. H. B. Shumacker Jr. and R. I. Lowenberg.—p. 79.
Treatment of Experimental Uremia by Intestinal Lavage. Beverly H. White and H. N. Harkins.—p. 90.
Neutralization of Heparin by Protamine. L. L. Cowley and C. R. Lam. —p. 97.
Patella Fractures: Method of Wiring. A. A. Michele and F. J. Krueger. —p. 100.
Use of Cancellous Bone Grafts for Small Defects of Skull and Brow Region. B. C. Martin.—p. 103.
Compound Transverse Fracture of Maxilla: Report of Case with Zygomatic Fixation. G. Cubero.—p. 109.
Effects of Supine Position on Ventilation of Lungs of Dogs. C. K. Drinker and Esther Hardenbergh.—p. 113.
Posterior Cisternal Drainage of Hydrocephalic Third Ventricle (Posterior Third Ventriculostomy): Preliminary Note. A. Schuller.—p. 119.

Pancreatic Secretion and Formation of Peptic Ulcer.—Poth and his associates studied the influence of the secretory activity of the pancreas on the formation of ulcers. Sixteen dogs were divided into four groups. Group I served as controls, group II was subjected to total pancreatectomy, group III had the pancreatic ducts ligated and group IV was made diabetic by the administration of alloxan. All of these animals received intramuscular injections of histamine in beeswax. Two control animals which were placed on the same feeding regimen as the dogs operated on had no symptoms of ulcer, and only 1 of them showed an ulcer after forty-five days. When the pancreatic secretion was diverted from the duodenum multiple severe ulcers developed. In both the ulcerations were much severer than have ever been observed in normal animals receiving histamine. It is obvious that the presence of the alkaline pancreatic juice in the duodenum is of great importance in the prevention of ulcers. Although removal of this secretion by extirpation of the gland does not of itself produce ulcers, it is apparent from the results of histamine stimulation that there is a strong predisposition to ulcer formation following pancreatectomy. These experiments do not indicate that diabetes exerts an inhibitory effect on the formation of peptic ulcers. The depancreatized animals were completely diabetic; yet ulcers developed in them just as rapidly and just as extensively as in the animals that had only the pancreatic ducts ligated. The alloxan-diabetic animals showed no lesser tendency toward induced formation of ulcer than did the normal controls. Removal of the pancreas or ligation of its ducts, as is frequently done in surgical procedures on the duodenum or pancreas, is not without danger of postoperative ulceration. It would seem to be advisable to reanastomose the pancreatic duct to the duodenum or jejunum whenever possible after resection of the head of the pancreas. It is doubtful that resection of the vagus nerve at the level of the diaphragm should interrupt a sufficient number of the parasympathetic fibers to the pancreas to alter significantly its secretion.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

56:377-432 (July) 1948

Additional Data in Technic of Vaginal Hysterectomy. N. S. Heaney. —p. 377.
Surgical Treatment of Congenital Pulmonary Stenosis: Tetralogy of Fallot. J. D. Stenstrom.—p. 386.
Neuro-Endocrine and Psychodynamic Factors in Sterility. H. B. Friedgood.—p. 391.
Congenital Intestinal Obstruction. S. F. Herrmann.—p. 399.
Consideration of Some Uterine and Ovarian Tumors. A. H. Curtis. —p. 404.
*Aberrant Pancreas in Meckel's Diverticulum Causing Intestinal Obstruction. R. R. De Nicola.—p. 407.
Primary Abdominal Pregnancy in Lesser Peritoneal Cavity. N. D. Elzey. —p. 410.
*Rupture of the Vaginal Vault During Coitus. A. W. Diddle.—p. 414.
Subacute and Chronic Nonsuppurative Thyroiditis. D. F. Brayton. —p. 417.

Aberrant Pancreas in Diverticulum Causing Intestinal Obstruction.—The case presented by De Nicola concerned a boy, aged 13, who suddenly became ill with severe constant pain in the lower part of the abdomen, associated nausea and vomiting, headache, high grade fever and profuse diarrhea. The abdomen was spastic throughout, mildly distended and tender, mostly on the left side. The patient was treated under the diagnosis of severe gastroenteritis, and conservative measures such as chemotherapy, intravenous administration of fluids and intestinal intubation saw him through a stormy course lasting two weeks. The patient had several similar attacks, each requiring hospitalization for weeks at a time. At a fifth attack signs of peritonitis were present and a laparotomy was done. A mass of purulent omentum and gnarled intestine was found low in the midline. The omentum was removed between paired clamps, and four or five loops of intestine were freed during the process. The right iliac fossa was explored and an acutely inflamed and markedly thickened appendix was found and removed. After the operation the patient remained well for several months, but later showed signs of intestinal obstruction. At operation an abscess containing approximately 10 cc. of pus surrounded a perforation in the intestine which was held to the posterior wall by a "nubbin" of tissue. Examination of the specimen removed showed it to consist of a segment of intestine the mucosa pattern of which was like that of the ileum. Heterotopic pancreas was seen in the wall of the intestine infiltrating the submucosal and muscular layers. The intestine and pancreas were both involved in scar and granulation tissue and were infiltrated with polymorphonuclear leukocytes and lymphocytes. Large pancreatic ducts were seen to be dilated as in obstruction. It is probable that the pancreatic ducts became blocked and that resulting cysts became secondarily infected to effect a coalescent abscess which caused both the ileac perforation and the obstruction.

Rupture of Vagina.—Diddle reports 2 women who sustained rupture of the vaginal vault during coitus. Including these 2 cases 133 major tears of the major vault resulting from coitus have been recorded in the past seventy-six years. Thirty-four subjects were previously virginal; 13 were patients having first sexual contact since delivery; 1 woman was pregnant, 8 were postmenopausal and 6 were having the first sexual contact subsequent to some gynecologic operation. Thus friability of tissues incidental to pregnancy and puerperium was etiologically involved in certain women. Two thirds of the tears involved the posterior wall or fornix and only four the anterior wall. Parametrial extension occurred twenty-one times. The peritoneum was exposed thirty times but was broken only six times. Four of these were in girls under the age of 12 years. The rectum was torn in 7, the bladder in 1. Eight incorrect diagnoses were made. They included abortion, carcinoma of the uterus and functional bleeding. Surgical repair was mentioned in 18 instances and tamponade in 20. Twenty-two of 133 patients died. Five of the 22 were young girls not fully mature, and 2 patients were postmenopausal. Seven died of sepsis and 2 of shock due to hemorrhage. Whether sepsis or shock accounted for the remaining mortalities was not ascertained. When vaginal tears involve the upper portion of the organ they may be overlooked because of inadequate visualization. The discussion emphasizes the value and the necessity of examination with a speculum.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

23:69-148 (June) 1948

Studies in Prematurity: Part 4, Development and Progress of Prematurely Born Child in Pre-School Period. C. M. Drillien.—p. 69.
Cause of Nuclear Jaundice in Neonatal Sepsis with Jaundice. J. I. De Bruyne and S. V. Creveld.—p. 84.
Cause and Significance of Seasonal Variations in Hemorrhagic Tendency in Newborn. E. Kerpel-Gronius, F. Varga and E. K. Pál.—p. 87.
Epidemic of Glandular Fever. F. R. Buckler.—p. 90.
Place of Oral Penicillin in Pediatrics. J. H. Mosely.—p. 93.
Amino Acids in Feeding of Infants. J. M. Smellie.—p. 98.
Septicemia of the Newborn: Clinical Study of 15 Cases. R. M. Todd.—p. 102.
Study of Neonatal Infections in Nurseries of Maternity Hospital. Muriel J. L. Frazer.—p. 107.
Occurrence of Edema in Infantile Gastro-Enteritis. J. Berkeley.—p. 114.
Giardia Lamblia: Incidence and Results of Infestation of Children in Residential Nurseries. E. H. Brown.—p. 119.
*Erb's Palsy. B. Wolman.—p. 129.

Erb's Palsy.—The term Erb's palsy is applied to that type of birth palsy in which the paralysis, or paresis, is confined to muscles supplied by the fifth and sixth cervical nerves. The deltoid, supraspinatus, infraspinatus, teres minor, biceps, brachialis, brachioradialis and supinator muscles are usually involved in cases of severe disease, whereas in cases of mild disease only some of these muscles are involved. Wolman reviewed the cases seen at the outpatients' department of a busy provincial teaching hospital during the last twenty-one years. Actually 125 persons with Erb's palsy presented themselves during that time, but the author has only been successful in tracing and interviewing 37 of this group. Injury at birth to the supraclavicular portion of the brachial plexus is the accepted cause of the condition. Skilled obstetric technic in delivery, particularly in the use of forceps, is the main factor in avoiding this paralysis. Large babies are more likely to be injured. A large child in a primigravida needs special care with the delivery of the head and arms. Treatment must be carried out from birth. Infants treated within the first month do well and results are 100 per cent successful. If treatment is delayed, contractures causing impaired function of the shoulder and elbow will develop quickly. The treatment consisted of adequate splintage, associated with massage, together with exercises in older children.

Brain, London

71:1-108 (March) 1948

*Microgliomatosis: Form of Reticulosis Affecting Brain. A. H. E. Marshall and F. B. Smith.—p. 1.
Gustatory Sweating. H. A. Haxton.—p. 16.
Influence of Alterations in Posture of Limbs on Cortically Induced Movements. E. Gellhorn.—p. 26.
Observations on Cutaneous Hyperalgesia, with Notes on Related Reactions. R. A. Harpman.—p. 34.
Central Mechanism of Some Optic Reactions. G. G. J. Rademaker and J. W. G. Ter Braak.—p. 48.
Electroencephalography with Pharyngeal Electrodes. J. Roubicek and D. Hill.—p. 77.
Distribution of Sympathetic Fibers in Brachial Plexus in Man. S. Sunderland.—p. 88.

Microgliomatosis.—Russell and her associates point out that Hortega and others have shown that the microglia represents the reticuloendothelial system in the central nervous tissue. The authors present a series of 7 cases of cerebral tumor in which the proliferating cells were predominantly of the microglial type. In 3 cases the cerebral tumors were associated with lesions of similar structure in other organs. It is considered that the character of the lesions in the brain and other organs justifies the classification of the condition as reticulosis. The authors cite a number of reports from the literature in which tumors are described which were similar to those in this series. It has been stated by some authors that tumors described as microgliomas are either gliomas or sarcomas, infiltrated by microglial cells. Such a view is untenable in the face of the evidence provided by the cases reported here. First, the existence of two tumors in which the great majority of the cells appeared to be impregnated and which showed proliferation of mature microglial cells at a distance from the main tumor; secondly, the presence in 3 cases of similar lesions in the spleen, lymph nodes and other tissues, and, thirdly, the gradation of intensity in the silver staining of the proliferating cells provide convincing evidence that these specimens are tumors of reticuloendothelial elements.

British Journal of Cancer, London

2:1-86 (March) 1948

Secondary Malignant Disease of Heart. R. W. Raven.—p. 1.
*Prognosis of Carcinoma of Breast in Relation to Type of Operation Performed. D. H. Patey and W. H. Dyson.—p. 7.
Excretion of 17-Kestoteroids in Men of Different Age-Groups, with Special Reference to Prostatic Cancer. A. M. Robinson.—p. 13.
Effects of Chloroethylamines on Tumors, with Special Reference to Bronchogenic Carcinoma. E. Boyland, J. W. Clegg, P. C. Koller and others.—p. 17.
Culture of Human Leukemic Blood Cells in Vitro. F. W. Gunz.—p. 29.
Incidence of Carcinoma in Transmissible Papillomatosis of Domestic Rabbit. F. R. Selbie and R. H. M. Robinson.—p. 48.
Observations on Nature of Estrous Cycle and on Effect on it of Milk Factor, in Mice of Two Inbred Strains, Differing in Mammary Cancer Incidence. E. C. Armstrong.—p. 59.
Biologic Tests with Cholesterol Esters of Unsaturated Acids. A. H. M. Kirby.—p. 70.
Factors Determining Action of Colchicine on Tumor Growth. R. J. Ludford.—p. 75.

Prognosis in Carcinoma of Breast.—Patey and Dyson compare the results of different combinations of surgical and irradiation treatment of carcinoma of the breast in a series of 118 patients treated between 1939 and 1943, and followed up until the end of 1946. He concludes that until an efficient general agent for the treatment of carcinoma of the breast is developed, a high proportion of patients are doomed to die of the disease whatever combination of surgical treatment and irradiation is used, because in a high proportion of cases the disease has passed outside the field of local attack when the patient first comes for treatment. A modified radical operation in which the pectoralis major is preserved shows results as good as those of the standard radical operation, and in addition has positive advantages. Wider sacrifice of skin with subsequent skin grafting is desirable to reduce the incidence of local cutaneous recurrences, which is still disconcertingly high. Partial mastectomy combined with axillary dissection may be justifiable in occasional early cases with small growths, but is unjustifiable as a routine, owing to the danger of local recurrence. Simple mastectomy combined with irradiation to the axilla may give a satisfactory result, but the irradiation is generally more upsetting to the patient than surgical dissection of the axilla.

British Journal of Venereal Diseases, London

24:45-88 (June) 1948

Treatment of Early Syphilis with Penicillin, Neoarsphenamine and Bismuth. G. L. M. McElligott, F. J. G. Jefferiss and R. R. Willcox.—p. 45.
*Significance of Pleuropneumonia-like or "L" Organisms in Non-Gonococcal Urethritis, Reiter's Disease, and Abacterial Pyuria. A. H. Harkness and A. Henderson-Begg.—p. 50.
Psychological Aspects of Venereal Disease. E. D. Wittkower.—p. 59.
Laboratory Aspects of Sexual Crime. H. S. Holden.—p. 68.
Laughlen Test with Particular Reference to Its Suitability as Preliminary Screen Test. B. R. Sandiford and Antoinette M. Khal.—p. 72.

Pleuropneumonia-like Organisms in Nongonococcic Urethritis.—Harkness and Henderson-Begg say that a number of organisms of the same group, usually referred to as pleuropneumonia-like or "L" organisms, have been described as causing arthritis, abscesses, pneumonia, "rolling disease" and other diseases. In recent years organisms of the group have been identified in the urogenital tracts of both men and women. The authors attempted to correlate the findings of pleuropneumonia-like or "L" organisms on culture with the different types of nongonococcic urethritis. Pleuropneumonia-like organisms have been cultured from 21 of 57 cases of subacute abacterial urethritis and from 5 of 10 cases of acute abacterial urethritis. "L" organisms were cultivated from urethral washings in 7 of 41 cases of arthritis complicating abacterial urethritis (so-called Reiter's disease). All cultures of joint fluid, blood, conjunctival secretion or cutaneous lesions were negative. "L" organisms were recovered from 2 of 74 cases of bacterial urethritis (nongonococcic), 2 of 16 cases of abacterial pyuria, 12 of 46 cases of nongonococcic cervicitis or vaginitis and 15 of 157 cases of acute gonorrhea. Fifty normal males and 15 normal females were also examined, but in no case were "L" organisms

recovered. Serologic investigations—agglutination and complement fixation—carried out on all suitable cases at varying stages of the disease were invariably negative in result. Thus, although evidence from cultures has favored the view that "L" organisms are etiologically related to certain types of abacterial urethritis, abacterial pyuria and possibly Reiter's syndrome, serologic tests have not supported this conclusion. Negative serologic reactions, however, cannot be regarded as strong evidence against the incrimination of "L" organisms in the causation of these diseases.

British Medical Journal, London

1:1121-1166 (June 12) 1948

*Pulmonary Valvulotomy for Relief of Congenital Pulmonary Stenosis: Report of 3 Cases. R. C. Brock.—p. 1121.
BCG Vaccination: Is It of Any Value in Control of Tuberculosis? A. Wallgren.—p. 1126.
*Efficacy of BCG Vaccination. H. Malmros.—p. 1129.
Exposure to D.D.T. A. Anderson and M. A. Khorram.—p. 1132.
Traumatic Pseudo-Cyst of Pancreas with Pleural Effusion: Report of 2 Cases. B. J. Bickford.—p. 1134.
Balanced-Pulsed Galvanism: Application of New Principle Avoiding Ionization Effects. C. E. G. Wickham.—p. 1136.

Valvulotomy for Congenital Pulmonary Stenosis.—The immediate results of the Blalock-Taussig operation can be dramatically successful, but two possible drawbacks suggest themselves: (1) that the fistulous communication may not grow with the child and thus will prove ineffective in later years; (2) that an arteriovenous leak or artificial ductus arteriosus is created—a condition for the relief of which, when it occurs as a congenital maldevelopment, an operation has been considered necessary. The relief of the obstruction itself would answer the greatest objection: An increased supply of blood would be provided to the lungs without the disadvantages of an arteriovenous leak. It is usually stated that the stenosis in these cases is almost invariably subvalvular or infundibular and is therefore not amenable to relief. This is not so; a number of patients with Fallot's tetralogy have valvular stenosis either with or without subvalvular stenosis; moreover, cases of morbus caeruleus occur in which a pure pulmonary valvular stenosis is present. The best way to assess the state of the valves is to inspect them under direct vision. The author describes 3 cases which show that pulmonary valvulotomy is a feasible operation, and all 3 patients have survived the procedure. The result in the first has been moderately successful so far; in the second the result is good; in the third it would appear to be good, but is as yet indeterminate functionally. The ages of the patients were 18, 11 and 23 years, respectively. Thus 2 patients were of an age when the prognosis is ordinarily poor. Far better results are to be anticipated in younger patients. The vascular complications are disturbing. The first case teaches that a careful watch must be kept for signs of peripheral arterial embolism after cardiotomy so that immediate embolectomy can be considered. Arterial thrombosis occurs also with the Blalock operation. Presumably it is most likely to occur when the blood pressure falls, especially in the presence of polycythemia. Much still remains to be done in the treatment of "blue children" with pulmonary stenosis, but the results are encouraging enough to justify proceeding further. This operation is not meant to supplant the Blalock operation. It is of use in only a small proportion of cases. Until a method can be found to relieve the subvalvular stenosis, the Blalock operation must continue to take precedence.

Efficacy of BCG Vaccination.—Malmros points out that last year hundreds of thousands of young children and adolescents in war-ravaged Europe were given tuberculin tests and that the nonreactors were vaccinated against tuberculosis with BCG. The statistically most trustworthy method of determining efficacy, that of vaccinating alternating patients, had to be abandoned in Scandinavia. In the author's district of Oerebro, Sweden, which has about 230,000 inhabitants, vaccination with BCG has been done extensively since 1942. Practically all the newborn are vaccinated. The whole population is gradually tuberculin-tested and the nonreactors are vaccinated if they give their consent. So far, 22,413 persons have been vaccinated, 8,040 being newborn infants, 7,836 children over 1 year, and 6,537 adults. When a patient is admitted to any hospital with the diagnosis of tuberculosis or suspected tuberculosis it is ascertained whether the patient has been vaccinated with BCG. By this means it is possible to find out whether any of those vaccinated have contracted tuberculosis. From 1942 to 1947 only 1 such case was discovered. The harmlessness of BCG is established beyond doubt. If Wallgren's method is used and the vaccine in a dose of 0.05 mg. is injected strictly intracutaneously, large abscesses seldom appear (0.8 per cent). Small abscesses occur in about 7.8 per cent. They heal relatively quickly. In newborn infants abscesses occur much more rarely (2.3 per cent) than in older children and in adults. The author states that the BCG campaign should not be confined to the newborn, but that whenever a nonreactor is encountered he ought to be vaccinated.

1:1167-1220 (June 19) 1948

*Lymphatic Connections of Subarachnoid Space: Experimental Study of Dispersion of Particulate Matter in Cerebrospinal Fluid, with Special Reference to Pathogenesis of Poliomyelitis. E. J. Field and J. B. Brierley.—p. 1167.
*Epidemiology of the 1947 Outbreak of Poliomyelitis in Eccles. W. P. Sweetnam.—p. 1172.
Ecology of Poliomyelitis in a Military Camp in 1947. G. J. Dixon.—p. 1175.
Aberrant Endometrial Tissue and Intussusception. E. M. Southern.—p. 1178.
*Neonatal Bact. Coli Meningitis After Prolonged Labor. H. R. Duval and J. T. Burrowes.—p. 1180.
Cervical Sympathetic Paralysis. J. D. Craig and R. C. Fuller.—p. 1182.
Day Nurseries and the Man-Power Problem. W. E. Cavenagh.—p. 1184.

Lymphatic Connections in Subarachnoid Space.—Field and Brierley say that suggestions have been made that infective agents, particularly the virus of poliomyelitis, may extend to the central nervous system along certain ill defined lymphatic pathways. The elucidation of direct anatomic pathways, particularly those between the spinal subarachnoid space and the abdominal lymphatic system, is taken up in this paper. After an outline of the salient features that have been presented in the literature, experiments on rabbits are described. Diagrams illustrate the mode of elimination of india ink particles from the subarachnoid cul-de-sac around the dorsal root ganglion of a spinal nerve; also from the subarachnoid extensions along the olfactory nerves. In both cases ink particles are eliminated from the subarachnoid space into interstitial tissue, and pass secondarily into the lymphatic system. The nasopharynx, tonsil and upper respiratory tract have all been implicated from time to time as portals of entry for virus. The results presented here have substantiated the existence of a definite anatomic pathway (in the rabbit) between the cranial subarachnoid space and the deep cervical lymph nodes by means of lymphatics which emerge through the jugular foramen. Since the tonsil, too, is connected with these nodes, the anatomic basis exists for lymphatic extension of virus from tonsil to cranial subarachnoid space. This connection is in addition to the more readily demonstrable paths from the nasal mucosa. The author also describes retrograde lymphatic flow to the cord. The prevertebral lymph nodes are the "regional" nodes of the spinal subarachnoid space. The presence of virus in the cerebrospinal fluid in human and experimental poliomyelitis would seem to be uncommon. In view of the rapidity with which particulate matter has been shown to be eliminated from the subarachnoid space, it is probable that reports in the literature are concerned with stages when virus, which has been present earlier, has already been eliminated. The distribution of fine particulate matter in the cerebrospinal fluid has been compared with that of the early lesions of poliomyelitis, and certain similarities have been noted suggesting that the fluid may play a more important part in the pathogenesis of the condition than that usually accorded it by adherents of the theory of neuronic transmission.

Epidemiology of Poliomyelitis Outbreak.—Sweetnam presents studies carried out in the course of an outbreak of poliomyelitis in Eccles in 1947. This borough had the highest attack rate of any district. There were 46 cases, giving an attack rate of 1.09 per thousand of the population. The case mortality was 6.5 per cent. The incubation period was seven to thirteen days. Only one family had more than 1 frank case. There was only 1 instance of a case to case contact. The epidemic was confined for nearly six weeks to the western half of the borough by a canal which restricted communications.

The results of field studies indicated that the chief factor in the spread of infection was human contact, in which abortive cases and healthy carriers played the major part. The presence of the virus in the nasopharynx of patients and carriers was of much more importance for the spread of infection than was its presence in feces. A survey revealed the presence of numerous abortive cases, especially in close proximity to frank cases, and suggested that of every 20 cases in which clinical signs and symptoms of infection were evident less than one developed into a paralytic case. Suggestions to improve the present system of notification are made, particularly the necessity for notifying abortive cases.

Neonatal Meningitis Due to Escherichia Coli.—According to Duval and Burrowes meningitis due to Escherichia coli is relatively more common in the newborn than in childhood or later life. The original portal of entry is difficult to determine, but there are indications that infection may enter at any of many sites. The following portals of entry have been mentioned: middle ear, intestine, lungs, genitourinary tract, spina bifida, umbilicus and morbid conditions of skin, scalp, mucosae and subcutaneous tissues. In addition, transplacental bacteremia, possibly arising from maternal pyelitis, has been suggested. Aspiration of amniotic fluid infected with Esch. coli, causing bronchopneumonia followed by spread through the blood stream to the meninges, has also been suggested as a portal of entry and seems to have been the route of infection in the fatal case reported here. The infant was 3 days old. The mother had intrapartum eclampsia and prolonged labor and on the third day of the puerperium contracted pyelitis due to Esch. coli and endometritis.

Journal of Tropical Medicine and Hygiene, London

51:111-132 (June) 1948

Prognosis in Schistosomiasis. M. Gelfand.—p. 112.
Studies in Tropical Ulcer: Part IV. Treatment of Tropical Ulcer. K. Hare.—p. 119.
Normal Lobular Neutrophil Picture in East African. K. E. Dewhurst.—p. 128.

Lancet, London

1:893-932 (June 12) 1948

*Control of Infection in Burns. L. Colebrook, J. M. Duncan and W. P. D. Ross.—p. 893.
Supernumerary Nipples and Neurosis. R. Harper.—p. 899.
Susceptibility to Cholera. S. Abdou.—p. 903.
Closing the Pneumonectomy Gap. G. S. Eedy.—p. 905.
Elliptical Human Erythrocytes in Egyptian Family. S. E. Kholy.—p. 908.
Partial Coarctation of Aorta with Bacterial Endocarditis and Bicuspid Aortic Valve. J. Bates and R. J. W. Rees.—p. 908.

Control of Infection in Burns.—Colebrook says that at the Birmingham Accident Hospital an attempt has been made to treat burns under conditions which aim at eliminating not only the "contact" infections (from hands, instruments), but also air-borne infections. Most of the sepsis of burns is due to infection in the hospital and can be prevented if the right conditions and the appropriate routine are established. Two distinct objectives have to be kept in view: (1) blocking the transmission of pathogens to the burns at the time of the dressing, and (2) blocking their transmission to the burns between one dressing and the next. The first of these objectives has been successfully attained during the three year period in the burns unit at the Birmingham Accident Hospital (734 patients treated) by having all dressings done by a trained team using a strict aseptic technic in a room ventilated by an abundant stream of filtered air. The number of patients infected with hemolytic streptococcus and pyocyanea at the time of dressing under these conditions has been less than 1 per cent. The second objective has proved much more difficult. The majority of the infections transmitted between one dressing and the next occurred in patients whose burns were difficult (or impossible) to cover adequately with dressings, or in patients who interfered with their dressings. When dressings become soaked with serous exudate during the first few days after burning, pathogens conveyed to the outer bandages from the air or from bedding are able to "grow through" the dressing and so infect the burned surfaces. The use of cellophane as a bacterial barrier to prevent this is suggested. Streptococcic infections have proved the easiest to control because they can be quickly eliminated from the burns by local application of penicillin (or of sulfonamide compounds). In view of the manifold opportunities for cross infections presented by a large ward and the highly infectable nature of burns, it is concluded that the best way to maintain a high level of freedom from hospital infection would be to nurse all burns during the first few weeks in well ventilated cubicles, each containing a single bed.

1:933-972 (June 19) 1948

Geographic Origin of Nurses. B. Woolf.—p. 933.
*Repair of Large Hernia with Tantalum Gauze: Experimental and Clinical Story. D. M. Douglas.—p. 936.
Leukemia Presenting with Neurologic Manifestations. W. R. Gauld.—p. 939.
Homologous Serum Hepatitis: Review of 216 Cases. D. Borensztein.—p. 941.
Chorionepithelioma Treated with Stilbestrol. S. Kullander.—p. 944.
Poliomyelitis and Associated Minor Illness in Residential School. J. C. Ryle.—p. 945.
Gangrene Following Intra-Arterial Injection of Myanesin with Study of Blood and Myanesin Mixtures. T. A. Ogilvie, J. B. Penfold and D. R. T. Clendon.—p. 497.
*Multiple Streptococcal Abscesses of Liver: Recovery with Penicillin. H. S. Morley.—p. 949.

Repair of Large Hernias with Tantalum Gauze.—Douglas describes reactions in rabbits in which sutures of tantalum, stainless steel, "inconel" (composed of 80 per cent nickel, 13 per cent chromium and 7 per cent iron), silver, black silk and surgical gut were implanted in the abdominal wall. It was found difficult to compare the tissue reactions to various suture materials because of the variation in response from animal to animal. Sutures of tantalum, stainless steel and "inconel" are associated with less tissue reaction than those of silk or of silver. The tantalum gauze which Douglas investigated was woven from tantalum wire of a diameter of 0.075 mm. It is sufficiently pliable to adapt itself to the movements of the abdominal wall. Segments of tantalum gauze were substituted for the whole thickness of the abdominal wall of rabbits and the repair was examined after 175 to 375 days. When an attempt was made to dissect the gauze from the abdominal wall, it became evident that the connective tissue fasciculi had grown through the meshes of the gauze. The tantalum gauze was used also in the repair of 32 large hernias in patients. These patients appear to have more pain in the first few postoperative days than do those who have had other types of repair. This may be due to the extensive dissection needed to obtain an adequate overlap. Of the 32 wounds, 3 became infected, whereas the others healed by primary union. The infected wounds all healed satisfactorily. One of the patients died of cerebral thrombosis three months after operation. All the other patients are in good health and have no complaints referable to the operation. The scars are soundly healed, soft and mobile, and the hernia has not recurred.

Penicillin in Multiple Streptococcic Abscesses of Liver.—Morley presents the case of a woman, aged 56, whose symptoms were considered as indicative of an anterior subphrenic abscess. At operation an enlarged liver presented itself, with surface studded with yellow raised areas, the mass felt being one of these. Aspiration yielded creamy pus which contained large numbers of streptococci. Penicillin, 100,000 units, was given forthwith, and thereafter 60,000 units every three hours for eleven days to a total dose of 4,060,000 units. On the third day of penicillin therapy temperature reached normal. The patient's general condition improved with unexpected rapidity, her pain subsided and her recovery was uneventful. Her doctor reported five months later that she was in perfect health.

Medical Journal of Australia, Sydney

1:665-696 (May 29) 1948

Goiter Studies: II. Relationship of Endemic Goiter to Food Consumption Pattern of Families. Anita Osmond and F. W. Clements.—p. 665.
Iso-Agglutinins in Cord Blood. Rachel Jakobowicz and Lucy M. Bryce.—p. 669.

1:697-724 (June 5) 1948

Technic of Aspiration Biopsy of Liver with Reference to Its Use in Diagnosis and Prognosis. W. E. King and J. W. Perry.—p. 697.
Some Aspects of Cholelithiasis and Obstructive Jaundice. I. J. Wood, W. E. King, P. J. Parsons and others.—p. 701.

Acta Clinica Belgica, Brussels

3:115-226 (March-April) 1948. **Partial Index**

Extrapleural Pneumothorax in Surgical Treatment of Pulmonary Tuberculosis. M. Berard and A. Duprez.—p. 117.
*Nitrogen Mustard in Treatment of Hodgkin's Disease, Polycythemia Vera and Myelomatosis. K. Iversen and K. Kjerulf-Jensen.—p. 138.
*Clinical Study of Treatment of Subacute Endocarditis. F. van Goidsenhoven and P. de Moor.—p. 151.
Encephalitis Caused by Vaccination in an Adult: Complete Cure After 21 Days of Coma. P. Govaerts.—p. 167.

Nitrogen Mustards in Hodgkin's and Other Diseases.—Iversen and Kjerulf-Jensen review observations on 21 patients who were treated with methyl-bis-(beta-chloroethyl)-amine-hydrochloride. The results were excellent in 6 cases of polycythemia vera. In 3 cases of multiple myeloma pain decreased, while in 5 of 9 patients with Hodgkin's disease symptoms were relieved, although this effect was only temporary.

Treatment of Subacute Endocarditis.—Seventeen patients with subacute bacterial endocarditis were treated by van Goidsenhoven and de Moor between September 1944 and June 1947 with penicillin alone or in combination with other therapeutic measures. As of Jan. 1, 1948, 12 of these patients are alive; 8 of these have completely recovered without signs of cardiac failure; in 3 the cardiac function has deteriorated more and 1 shows severe cardiac failure but no signs of infection. For 2 of the 5 patients who died, the treatment was not sufficient, because of the shortness of the supply of penicillin (in the period 1944-1945); in 1 case the treatment started too late (after one hundred and thirty weeks' evolution). The last 2 cases proved refractory to a normally adequate treatment. The authors propose as a routine treatment: for the first two days twelve to sixteen times 100,000 or 200,000 units of penicillin in twenty-four hours; for a period of four weeks eight times 100,000 units of penicillin per day and, finally, a two week period with eight times 50,000 units per day. If symptoms of infection do not disappear with this treatment and the blood cultures still remain positive, the therapeutic plan has to be completely modified. The doses will then be based only on the in vitro sensitivity of the isolated germs and on the penicillin levels in plasma.

Archivos Inst. de Cardiología de Mexico

18:345-450 (July 31) 1948. **Partial Index**

*Diastolic Extra-Sounds and Gallop Rhythm: Graphic Characteristics, Frequence, Clinical Importance and Audibility in Normal Persons and Cardiac Patients. A. A. Luisada and M. Roitman.—p. 345.

Diastolic Adventitious Sounds and Gallop Rhythm.—Luisada and Roitman studied 111 phonographic tracings of 90 persons, either normal or with cardiac disease, at the Instituto de Cardiología of Mexico. Adventitious sounds were encountered in 72 per cent of normal persons and in 52 per cent of patients with cardiac disease. Gallop rhythm was found in 28 per cent of the former and in 48 per cent of the patients with cardiac disease. Having found that no single criterion is sufficient for differentiation of adventitious sounds from gallop, they established the following arbitrary rule as a result of the study: (*a*) A vibration having a frequency of 30 or more per second was called gallop whatever its height. In almost all such cases the height was found to be two thirds or more that of the normal heart sounds. (*b*) A vibration having a frequency of less than 30 per second was considered a gallop only if its height was greater than two thirds of that of the normal heart sounds. (*c*) A vibration having a frequency of less than 30 per second and a height lower than two thirds of that of the normal heart sounds was considered as an adventitious sound. Comparison between clinical auscultation and phonocardiographic findings reveals that no relation exists between them. The multiple causes of error inherent in clinical auscultation emphasize the importance of phonocardiography. While adventitious sounds and gallop rhythm are more frequent in cardiac patients than in normal persons, they may be found occasionally in the latter, as their production is favored by functional elements which may be present in the absence of heart disease and among which tachycardia is one of the most common. The phonocardiographic classification proposed does not separate physiologic from pathologic cases even though it facilitates grading of the severity of the functional disorder of the heart. There are gallops which are inaudible, and their detection by phonocardiography is important for complete evaluation of the clinical data.

Helvetica Medica Acta, Basel

15:223-318 (June) 1948. **Partial Index**

*Pathogenesis and Etiology of Evanescent Pulmonary Infiltrations with Blood Eosinophilia (Löffler's Syndrome). W. Löffler, A. F. Essellier and M. E. Macedo.—p. 223.
Influence of Liver on Synthesis of Lipoproteins in Blood. F. Reubi.—p. 262.
Action of Embryonal Liver Extract on Normal Antibodies. L. Goreczky and I. Csefkó.—p. 281.
*Influence of Temperature on Takata Reaction. H. Baur.—p. 285.
Coagulation Defect of Hemophilic Blood. W. Meier.—p. 304.

Pathogenesis of Löffler's Syndrome.—A review of the literature convinced Löffler and his associates that so far no indisputable proof has been furnished that ascariasis is the cause of the evanescent pulmonary infiltrates with eosinophilia first described by Löffler in 1932. A number of investigators, including Löffler, found that it is a causal factor in some of the cases. In this report the authors describe animal experiments which were designed to clarify the question regarding the causal significance of ascariasis. A total of 48 guinea pigs was used in two experiments. It was possible to reproduce in every detail the syndrome of evanescent pulmonary infiltration with eosinophilia, and it was possible to corroborate the observations of other research workers. The authors were able to demonstrate the larvae of Ascaris in eosinophilic infiltrations. Their pathologic observations confirm the observations made by von Meyenburg and Nagel in human subjects. The authors direct particular attention to the hitherto ignored atelectasis, which is important in the pathogenesis of the evanescent pulmonary changes. They also stress that the localization of the eosinophilic infiltrations does not permit conclusions regarding the portal of entry or the nature of the causal agent.

Cold Temperature and Takata Reaction.—The observation that the Takata reaction was more frequently positive during the cold season induced Baur to study this reaction under refrigerator temperatures (average of plus 3 C.). It was found that cooling healthy subjects or their blood for a short time had no influence on the outcome of the reaction. In cases of parenchymal disease of the liver verified at necropsy the Takata reaction was occasionally negative when the test was done at room temperature, but became positive when it was done at refrigerator temperature. Furthermore, in the course of hepatic disease the "cold" Takata reaction becomes positive sooner and remains so longer than if the test is done at room temperature.

Helvetica Paediatrica Acta, Basel

3:167-252 (July) 1948

Achylic Chloranemia During Childhood (Essential Hypochromic Iron Deficiency Anemia with Achlorhydria). C. Gasser.—p. 167.
Isolated Case of Pleonosteosis Léri. H. Zellweger.—p. 199.
Two Cases of Dysostosis Morquio (Differentiation from Dysostosis Multiplex). H. Zellweger and M. Schaichet.—p. 208.
Acute Infectious Lymphocytosis (Institutional Epidemic in Children). E. Martens.—p. 220.
Lymphoblastoma of Small Intestine in Child of 4 Years. F. Thélin and J. de Rougemont.—p. 225.
*Urethane in Treatment of Acute Leukemia in Childhood. R. F. Landolt.—p. 232.

Urethane in Leukemia of Children.—Landolt reports studies on 16 children who ranged in age up to 11 years, and who had acute leukemia. The children were treated with urethane, which is an ethyl ester of carbamic acid. The substance was given orally or by rectum in doses of 1 to 3 Gm. per day. Except for isolated cases of vomiting, there were no unpleasant secondary effects. The leukocyte count dropped to 500 or less within from five to ten days. The proportion of neutrophils rose considerably in some cases, but only rarely would a small absolute increase be shown. Increased erythropoiesis in the bone marrow was noted in 5 of the children; in 4 of these it was slight and in 1 great. There seemed to be an increase in the number of mitoses under the influence of the urethane. The swelling of the liver, spleen and lymph nodes decreased in 10 of the patients, in some of them decidedly, and there was a simultaneous improvement in the general con-

dition. The favorable effect on the clinical state was only temporary. In one patient all leukemic changes subsided and panhemocytophthisis developed. Four other cases showed the same tendency, without, however, reaching a point where complete regression of the extramedullary leukemic foci occurred. Urethane apparently can damage erythropoiesis and thrombopoiesis. Urethane therapy can be recommended in acute leukemia, since improvement can take place, but it is necessary to check the blood picture so that the preparation can be discontinued before panhemocytophthisis sets in. The author recommends simultaneous employment of penicillin, in order to prevent infection, and advises frequent blood transfusions to counteract the development of panhemocytophthisis.

Journal de Médecine de Lyon

29:453-490 (July 5) 1948. **Partial Index**

*Statistics of Infectious Endocarditis Treated with Antibiotics (Penicillin and Streptomycin). P. Sédallian, P. Monnet, M. Vialtel and R. Maral. —p. 453.
*Acute Miliary Tuberculosis Treated with Streptomycin. P. Sédallian, J. Moinecourt, M. Vialtel, R. Maral and others.—p. 461.

Antibiotics in Infectious Endocarditis.—Sédallian and his co-workers treated 24 patients with infectious endocarditis by intramuscular administration of penicillin and treated 6 additional penicillin-resistant patients with streptomycin. Eighteen patients recovered and there were 12 failures including 11 deaths and 1 patient whom the persistent infection induced to leave the hospital. Pending laboratory results, treatment should be instituted with large doses of penicillin (1,000,000 to 1,500,000 Oxford units). In cases with negative laboratory results the same high doses should be employed for at least ten to fifteen days, and then should be reduced according to the improvement obtained. The dose should be based on the results of the laboratory tests; it should insure a blood level three or four times superior to that of the microbic resistance. Duration of the treatment depends on the symptoms and their clinical evaluation. In 7 of 8 patients with negative blood culture the treatment failed, but 3 of 4 in whom penicillin was ineffective recovered when streptomycin was given. Penicillin was effective in 13 of 15 patients with Streptococcus viridans. A temporary resistance to penicillin subsided in some of these cases after temporary discontinuation of the drug: with this method the prospects are better than when progressive doses are employed, which will only exaggerate the resistance to the drug. Penicillin was ineffective in 3 cases with Enterococcus, but in 1 of them recovery was obtained with streptomycin. Synergistic action of penicillin and streptomycin was not apparent in any of the authors' cases. Streptomycin is indicated for cases in which an acquired resistance to penicillin is due to insufficient treatment.

Streptomycin in Miliary Tuberculosis.—Sédallian and his co-workers treated 49 patients with miliary tuberculosis with streptomycin. None of them presented any meningeal symptoms on admission to the hospital. In 17 the disease was severe, with high grade fever, dyspnea and cyanosis. Twenty patients had fever of long duration without pronounced functional symptoms. Twelve patients had afebrile miliary tuberculosis or were running a temperature around 38 C. (100.4 F.). Thirteen patients had genitourinary lesions; 9 had laryngeal lesions, and 26 had pulmonary lesions. Results showed that the patients remained tuberculous and the course of their disease differed according to its localization, as it did before streptomycin was instituted: the genital lesions showed a tendency to total or subtotal regression, particularly in women; the pulmonary lesions showed a tendency to stabilization, to cavity formation, fibrosis or caseation depending on the case. The streptomycin cicatrized the laryngeal lesions, reduced the pulmonary congestion or perifocal inflammation and was responsible for the disappearance of the minute tubercles in the roentgenograms. Koch's bacilli did not disappear; their caseating and fibrotic effect was not changed. Their behavior seemed to depend on the normal reaction of the various tissues. The disappearance of the minute tubercles in the roentgenograms is only an episode in this diffuse hematogenous disease which threatens the meninges. Proper dosage and continued treatment for three to four months may be life saving in those cases in which the meninges were not yet involved when treatment was instituted. Early symptoms must be watched for, and ophthalmologic signs are of great importance because lumbar puncture is not without risk.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

92:1365-1436 (May 8) 1948. **Partial Index**

Modern Hearing Aids. W. J. Pothoven.—p. 1375.
Simplified Determination of Acetone in Urine According to Rabinowitch. E. Sangster.—p. 1379.
*Is it Advisable to Treat Tonsillitis with Sulfonamides? H. A. Voet. —p. 1380.
*Uremia as Result of Sodium Chloride Deficiency in Pregnancy and Puerperium. G. A. Lindeboom.—p. 1384.

Advisability of Sulfonamide Drugs in Tonsillitis.—Voet compared two groups of patients with tonsillitis, one of which had been treated before the time sulfonamide drugs were generally used and the other was treated with sulfonamide drugs. No shortening of the duration of the disease or of the fever could be noted in the patients who had been treated with sulfonamide compounds. The author warns against routine chemotherapy in patients with tonsillitis, for not only is there a danger that toxic effects and hypersensitivity might develop, but the bacilli may become resistant to chemotherapy, and thus the sulfonamide compounds may lose their effectiveness.

Uremia After Salt-Deficient Diet in Pregnancy.—Salt-free or salt-deficient diet is often prescribed for pregnant women, particularly if edema or increase in blood pressure suggests a possible renal defect. The author presents the histories of 4 women, which indicate that deficiency in sodium chloride may lead to uremia in pregnant or puerperal women. One of these women had been subject to hyperemesis throughout her pregnancy. The other 3, however, had been on a salt-free diet. These cases demonstrate that a salt-free diet, although helpful in some cases, is not entirely without danger, particularly if it is continued over long periods. The renal function becomes impaired by the sodium chloride deficiency and the complete restoration may require months.

Nordisk Medicin, Stockholm

38:1063-1110 (May 28) 1948. **Partial Index**

*Blood Findings in Juvenile Amaurotic Idiocy. K. v. Bagh and H. Hortling.—p. 1072.
Diphtheria Treated with Serum Containing Antitoxin and Antibacterial Antibodies. A. Kåss.—p. 1076.
Congenital Clubfoot. J. A. Böök.—p. 1080.
Injury to Brachial Plexus Following Anesthesia. K. Liavaag.—p. 1081.
Critical Viewpoints Concerning Palliative Resection in Duodenal Ulcer. S. Lindgren.—p. 1084.

Blood Findings in Juvenile Amaurotic Idiocy.—Blood studies of 6 patients with this disorder revealed abundant vacuole formation in the lymphocytes in cytoplasm otherwise apparently normal. Vacuolated lymphocytes, van Bagh and Hortling state, were fewer in recent cases than in those of longer standing. In the sternal punctate, without other pathologic cell elements, the vacuolated lymphocytes were less numerous than in the peripheral blood. Attempts to stain the vacuoles by different staining methods failed. The vacuoles did not appear in dark ground illumination. The occurrence of highly vacuolated lymphocytes is believed to be significant in the establishment of juvenile amaurotic idiocy. The vacuolation is assumed to be due to a disturbance in the vital function of the mature lymphocytes, possibly dependent on disturbance in lipid metabolism.

38:1211-1246 (June 18) 1948

Pathogenesis of Essential Hypertension. H. Laake.—p. 1211.
Sahli's High Pressure Stasis. T. Friis.—p. 1214.
*Treatment of Cold Feet and Legs After Poliomyelitis. K. Stenport. —p. 1217.
Adrenal Cholesterin and Effect of Testerone on Adrenal Cortex. C. G. Bergstrand.—p. 1219.
Temporary Hypertension After Vagus Resection. J. M. Marcussen. —p. 1222.
Effect of Arteriovenous Anastomosis on Hypertension. H. Fabritius. —p. 1223.
Sensitiveness to Penicillin. H. K. Kristensen.—p. 1224.

Treatment of Cold Feet and Legs After Poliomyelitis.—Stenport says that cold feet and legs, with blue discoloration of the skin, are a frequent sequel of poliomyelitis. Treatment with a vasodilating substance, 2-benzylimidazoline hydrochloride

("vasodil") was carried out in 1944 in a large number of cases and as a rule resulted in a more or less transient sensation of warmth. After preliminary blocking of the second and third lumbar ganglions with 1 per cent procaine hydrochloride showed positive results, sympathectomy of the second and third lumbar ganglions was done in 90 cases from 1945 to 1947 with good primary results both subjectively and objectively. The surgical treatment is reserved for cases with pronounced vasospastic changes in which repeated treatment with the drug is ineffective and in border cases in which this treatment gives only partial relief.

Presse Médicale, Paris

56:469-484 (July 3) 1948

First Trials on Therapeutic Value of Pyroligneous Oil. A. Lemaire, J. Loeper and E. Housset.—p. 469.
Comparative Study of Agglutination Power of Serum and Tuberculin Tests After Vaccination with BCG by Scarifications. R. Sohier. —p. 470.
*Some Problems Involved in Treatment of Abscess of Lungs with Intrabronchial Penicillin. H. Métras, M. Grégoire, J. Lieutier and C. Gaillard.—p. 471.

Intrabronchial Penicillin in Pulmonary Abscess.—Métras and his co-workers treated 60 patients with pulmonary abscess with penicillin by intrabronchial route. In cases of severe disease it was combined with systemic penicillin therapy, 1,000,000 units per day. Recovery from pulmonary abscess may be considered complete (1) with the disappearance of functional symptoms and return to health as demonstrated by bronchography within six months after last subjective symptoms; (2) with mild roentgenologic or bronchographic sequelae within two years after last functional symptoms, and in the absence of hemoptysis and expectoration. Recovery of the first type was obtained in 30 patients and of the second type in 15 patients; i. e., 75 per cent recovered, while 15 patients (25 per cent) failed to recover, 6 because of extrapulmonary causes. The remaining 9 patients had recurrence after penicillin was discontinued; they required pulmonary surgical treatment, which is probably less dangerous after treatment with penicillin. Results of intrabronchial penicillin treatment for pulmonary abscess are superior to those of pneumonotomy reported by Neuhof and Tourrof in 1944.

Semaine des Hôpitaux de Paris

24:1609-1650 (July 2) 1948. **Partial Index**

*Semeiologic Importance of Electroencephalography in Diagnosis of Epileptic Attacks in Children. L. Cornil, A. Cremieux and H. Gastaut. —p. 1609.
Results and Accidents of Treatment of Certain Types of Tuberculosis with Streptomycin. C. Mattei.—p. 1614.
*Necrotic and Suppurative Forms of Primary Cancer of Lung (Anatomic and Pathogenic Study). R. Poinso, Y. Poursines, J. Charpin and P. Martin.—p. 1618.
*Chemical Pregnancy Test: Determination of Sodium Pregnandiol Glycuronidate. R. Rivoire and G. Bueil.—p. 1634.

Electroencephalography in Diagnosis of Epilepsy in Children.—Cornil and his co-workers made electroencephalograms of 184 children between the ages of 6 and 13 years, 138 of whom had clinical epilepsy, while in 46 the epilepsy was doubtful from the clinical point of view. A typically normal tracing, taking into account the age of the child, furnishes a presumption against the diagnosis of epilepsy, but does not provide definite proof. Positive diagnosis is made in the presence of two conditions: (1) when during rest one observes paroxysmal waves characterized by considerable amplitude, by their rhythmicity and sometimes by their regularity. Jasper's term of "hypersynchronic rhythm" seems to be appropriate because these rhythms are very likely due to an excessive synchronization of the cortical neurons; (2) when one observes a slow dysrhythmia which is incompatible with the age of the patient, in a child with nervous attacks of a definite or nearly definite epileptic nature. Electroencephalographic confirmation of the diagnosis of epilepsy was obtained in 90 per cent of the patients in whom clinical diagnosis of epilepsy was made. Probability of epilepsy is suggested every time when a definitely pathologic tracing has been obtained which is not specific for epilepsy in a child presenting nervous attacks the epileptic nature of which has not been established clinically. Such pathologic tracings are represented in general by a slow dysrhythmia incompatible with the age, or by continuous or paroxysmal slow hypersynchronous waves which may be elicited by hyperpnea in a child with considerable glycemia. The possibility of an epileptic process should be considered when one observes a pathologic nonspecific tracing in a child presenting nervous attacks whose epileptic nature appears unlikely from the clinical point of view.

Necrotic and Suppurative Forms of Pulmonary Cancer.—According to Poinso and his co-workers, the destruction of the pulmonary tissue and the resulting suppuration which occur in the course of primary cancer of the lung may be explained by the obstruction of the bronchial arteries due to the accumulation of cancerous cells. These necroses occur particularly in cases in which the tumor is located in the hilus. The necrosis may result in formation of a cancerous cavity, or it may be limited to the periphery of the cancer, for which the term extraneoplastic necrosis is suggested. The latter type is responsible for the large suppurative ulcerations which may involve one or several lobes. Infection may be limited or completely absent, and that confirms the necrotic origin by obliteration of the bronchial arteries. When infection is present, it is limited to the peripheral crown of the destroyed zone, and therefore may be considered as secondary. In case of primary infection a massive polynuclear reaction should have been observed in the center of the destroyed area, but was not in the cases studied by the authors.

Sodium Pregnandiol Glycuronidate Test for Pregnancy.—Rivoire and Bueil describe a new rapid and simple technic for the determination in the laboratory of sodium pregnandiol glucuronidate, half the amount of the urine excreted within twenty-four hours (about 500 Gm.) and iso-amylic alcohol for the extraction being used. The final determination is made by nephelometry. The determination of sodium pregnandiol glucuronidate is an excellent test for pregnancy. It has the advantage of not requiring animal experiments. It is as valuable as Friedman's test, the performance of which may require forty-eight hours as compared with three quarters of an hour for the pregnandiol test. In gynecology the usefulness of the determination of sodium pregnandiol glycuronidate is of the first order, but its utilization is limited by material difficulties because repeated analyses are indispensable for the complete exploration of the menstrual excretion of pregnandiol.

Wiener klinische Wochenschrift, Vienna

60:393-412 (June 25) 1948. **Partial Index**

Colorimetric Determination of Aromatic Amidine in Urine. F. Lieben. —p. 393.
Histidine and Histamine Metabolism in Normal and Toxemic Pregnancy. Regine Kapeller-Adler.—p. 395.
*One Case of So-Called "Voluntary" Acceleration of Pulse with Reverse Accentuation of Cardiac Sounds. F. Scheminzky.—p. 398.

"Voluntary" Acceleration of Pulse.—Scheminzky reports a man between 40 and 50 years old presenting himself at the Vienna Physiologic Institute for demonstration, who was able to bring some of his skeletal muscles into action and who could influence at will his heart beat. By word of command such as "quicker" or "slower" he gradually produced changes in the pulse rate. During tachycardia the pulse rate was increased to double that during rest, reaching a maximum of 123 per minute. Slowing of the pulse rate was manifested as diminished tachycardia, and the minimum reached varied from 57 to 51 per minute and was not much below the starting point at the beginning of the experiment. During bradycardia, on complying with the command "slower," Valsalva's experiment was always associated with a reversion in the accentuation of the cardiac sounds: it was always the first cardiac sound which was louder, while the second cardiac sound was louder and therefore more accentuated during rest and during tachycardia. The reversed accentuation of the cardiac sounds, a sequel of the impaired filling of the heart during bradycardia, is of interest with regard to the pathogenesis of the first cardiac sound in mitral stenosis.

Book Notices

Medical Hypnosis. Volume I: The Principles of Hypnotherapy. Volume II: The Practice of Hypnotherapy. By Lewis R. Wolberg, M.D., Assistant Clinical Professor of Psychiatry, New York Medical College, New York. Fabrikoid. Price, $5.50; $6.50. Pp. 449; 513. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1948.

This book represents probably the most thorough, comprehensive, up-to-date exposition on the history, technic, applications and therapeutic goals of hypnosis published up to the present time. In the preface to volume I, the author states: "Few therapies in the history of medicine have enjoyed simultaneously such widespread acclaim and such universal condemnation as has hypnosis. To some extent these opposing attitudes still prevail. However, recent years have witnessed advances in experimental and therapeutic hypnosis which have tended to establish hypnotherapy firmly as a scientific treatment method.

". . . The teaching of any psychotherapeutic method is best achieved by personal observation and practical experience. For this reason, the manner of presentation in these volumes is somewhat unique. A considerable portion of Volume One is devoted to a step-by-step description of the induction process, illustrating various induction methods by excerpts from transcriptions of actual hypnotic sessions. There is a didactic discussion of the principles of psychotherapy, and of the psychopathologic factors in the different disease syndromes.

"Volume Two contains three complete transcribed case histories which enable the reader to follow the various stages in treatment, and to observe the therapeutic management of the patient as if he were personally present at the sessions from the beginning to the end of therapy. In each instance, these illustrate a preceding discussion of the uses and limitations of the chief short-term psychotherapeutic methods.

"Hypnosis adds speed and directness to psychotherapy, but it must not be regarded as a cure-all. A number of emotional problems fail to respond to hypnotherapy and require traditional long-term analytic approaches.

". . . While books such as this work are helpful, and constitute a convenient guide, they merely indicate the lines along which the physician may develop his therapeutic skills. Practical experience, particularly in some psychiatric training center, is indispensable in permitting of a full development and utilization of available therapeutic aptitudes."

In the preface to volume II, the author states: ". . . The present volume describes the joint technics of hypnosis and psychotherapy by presentation of actual case material through complete transcription of a number of treatment sessions. In addition to several briefer examples, three complete psychosomatic cases are included, illustrative of the three main divisions of therapy presented in this volume.

"The conclusions which have been presented in each of the three types of therapy — symptom removal, psychobiologic therapy and psychoanalytic therapy — are based on clinical experience with a fairly wide variety of cases. As more experience is gained in the different treatment methods, however, a modification and revision of these conclusions will undoubtedly be required."

These quotations accurately indicate the contents of this well written, well organized book. There is an excellent bibliography placed at the end of each chapter and a good adequate index. This book is recommended reading for every psychotherapist whether or not he employs hypnosis in his professional work.

Practice of Allergy. By Warren T. Vaughan, M.D. Second edition revised by J. Harvey Black, M.D. Fabrikoid. Price, $15. Pp. 1132, with 333 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

This book by the late W. T. Vaughan is generally considered one of the best textbooks and standard reference books on the subject. In the preface of the second edition, J. Harvey Black expresses the difficulty of carrying on the tradition established by its original author. The reader senses that Vaughan's vast experience and indefatigable search for knowledge on the subject are lacking. This becomes apparent from a cursory glance at the otherwise extensive bibliography, which contains relatively few recent references in spite of the abundance of new material on the subject.

This edition follows the outline of the previous one, the highlights being the chapters on food, fungi and pollen, which are most comprehensive and remarkably well illustrated. The part on pollen especially, written by O. C. Durham, the recognized authority on the subject, is excellent. Such important contributions to allergy as antibiotic therapy or the new theories concerning the allergic background of the collagen diseases are only casually mentioned or omitted entirely. On the psychosomatic aspect of allergic diseases, further elaboration would be desirable. Little is said about complications of asthma and nothing on the subject of the rehabilitation of the asthmatic patient. While there is an adequate chapter by J. B. Howell on local treatment of fungous diseases of the skin, no mention is made of local measures for atopic eczema. In treating hay fever, the most effective means of properly gaging the doses is not stressed; namely, the observation of the degree of local edema from each injection. In coseasonal treatment, few allergists follow the practice of administering 0.3 cc. of epinephrine with the pollen extract. The important subject of urticaria and angioneurotic edema is confined to four pages. More detailed elaboration on the therapeutic management of the individual allergic diseases would have been more useful than a chapter on pharmacology of allergy.

In spite of these minor criticisms, this book remains one of the most valuable textbooks on the subject. The material is most authoritative and instructive. The book is well printed and well indexed. It is indispensable to any one interested in allergic diseases.

Modern Trends in Dermatology. Edited by R. M. B. MacKenna, M.A., M.D., F.R.C.P., Physician in Charge, Dermatological Department, St. Bartholomew's Hospital, London. Cloth. Price, $8.50. Pp. 432, with 32 illustrations. Paul B. Hoeber, Inc., 49 E. 33rd St., New York 16, 1948.

This excellent volume is a collection of eighteen articles on recent advances and knowledge relating to dermatology. The majority of chapters have been written by outstanding specialists in collateral branches of medicine. The wisdom of this choice is evidenced by the ability of these authorities to assess scientifically the value of new discoveries in their special subjects. Although primarily written for the dermatologist, this book also serves to clarify some of the interrelationships between dermatology and internal medicine.

The volume is introduced by a brilliant chapter on the mechanism of research, emphasizing the need for fundamental thinking and creative work in functional fields. How wide is the abyss between the gifted observer of the commonplace and the sterile case reporter of one more unimaginatively studied and unimportant rarity! The chapter on nutrition is written with disarming candor. In it, Marrack states that while the treatment of some diseases of the skin with vitamins may be beneficial in a higher series of cases than can be ascribed to chance, the effect of such treatment is uncertain. He urges a more careful analysis of strictly clinical reports of improvement following vitamin therapy in order to diminish the vast and usually vague therapeusis in this field.

Two thought-provoking sections in this book are new and welcome strangers to the dermatologic literature. The first, in discussing the prevention of cutaneous disease, states that dermatologists must be students of human and social biology inasmuch as the living organism responsible for many diseases of the skin is neither a mite nor a coccus but man, himself. The second unique section embodies programs devised by the British Army to rehabilitate patients suffering from cutaneous disease.

Although the majority of chapters are thorough and adequate, especially those on hormones and the interpretation of statistics, others require modification in order to prevent unnecessary overlapping and the repetition of well known facts. It is always advisable for collaborators to read one another's articles. The chapter on radiation therapy is uncritical and overly optimistic. For example, the author states that roentgen therapy is effective in psoriasis but neglects to add the words "temporarily and cautiously." The section on therapy is only fair. The surveys of physiology and functional pathology review much recent investigative material but are repetitive and could well be combined with the chapter on anatomy. Many of the aforementioned

research projects clearly show that human skin differs so profoundly from that of other animals in structure, function and therapeutic response that one can learn about it only from studies on human beings.

In general, the book is a timely and comprehensive study of dermatologic knowledge. It should be of lasting value to dermatologists and senior students of dermatology.

Thérapeutique par la pénicilline. [Le premier Congrès française de la pénicilline, 1946.] Ministère de la santé publique, Service central de la pharmacie. Paper. Pp. 894, with illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1947.

In the United States 21,491 billion units of penicillin were produced during the first three months of 1948. In the same period in 1947, the output was 7,780 billion. This great increase in output reflects two things; first, more and more penicillin is being used by physicians for the treatment of infections and, secondly, it continues to be the most potent chemotherapeutic agent for the treatment of a wide variety of infections.

In April 1946 a congress was held in Paris to discuss the results of the application of penicillin in France. This four day meeting was sponsored by the Minister of Public Health, Dr. Cavaillon, and the various papers presented are now available in this 894 page book. The first part consists of four chapters on general reports of interest to internists, surgeons and their respective specialties. The second part gives the detailed studies of many physicians throughout France in a variety of infections. The third part is a statistical summary of the results. The papers present clearly what can be accomplished with penicillin in relatively low doses. There are a great many well documented case reports. For all physicians interested in the application of penicillin, this monograph can be recommended for purposes of reference and reading.

The 1946 Year Book of Neurology, Psychiatry and Neurosurgery. Neurology. Edited by Hans H. Reese, M.D., Professor of Neurology and Psychiatry, University of Wisconsin Medical School, Madison, and Mabel G. Masten, M.D., Associate Professor of Neuropsychiatry, University of Wisconsin Medical School. **Psychiatry.** Edited by Nolan D. C. Lewis, M.D., Director, New York State Psychiatric Institute and Hospital, New York. **Neurosurgery.** Edited by Percival Bailey, M.D., Professor of Neurological Surgery, University of Illinois, Chicago. Fabrikoid. Price, $3.75. Pp. 732, with 103 illustrations. The Year Book Publishers, 304 S. Dearborn St., Chicago 4, 1947.

The 1946 Year Book of Neurology, Psychiatry and Neurosurgery represents a gallant effort to keep abreast of the rapidly mounting volume in these three disciplines. The abstracts have been carefully selected, but the limitations of space precluded the inclusion of a number of important contributions. Of the 709 pages, 292 are devoted to neurology, 247 to psychiatry and the remainder to neurosurgery. Perhaps the allotment of space in the three categories is somewhat disproportionate. At least as much space might have been given to psychiatry as to neurology. The distribution of subjects in the field of psychiatry is rather good—general topics, child psychiatry, schizophrenic reactions and other psychoses, organic reactions, toxic psychoses, psychoneuroses and psychosomatic disorders, military psychiatry and special therapy. Probably the psychoanalysts will feel that psychoanalytic literature has been treated in stepchildish fashion. The references to psychoanalytic literature are few. The Quiz Section, which is an added feature, lends itself more naturally and readily to neurologic and neurosurgical subjects than to psychiatry. In the first two categories, information is often concrete enough to admit of more or less definite questions and answers. While the body of psychiatric information is considerable, it does not lend itself well to streamlined questionnaires, and treatment on this level is not favorable to a rapidly developing discipline.

It would seem desirable to publish two Year Books, one for neurology and neurosurgery, and the other for psychiatry. Among other things, this plan would give psychiatry more much needed space. Furthermore, it would permit more consideration of the psychiatric implications of internal medicine, pediatrics and the other subdivisions of medicine and surgery with which psychiatry now has such an intimate and productive liaison, at least as fruitful as the contacts with neurology and neurosurgery. Despite faults, largely due to trying to encompass the review of three important subjects in too few pages, the Year Book is a meritorious achievement.

Teaching Psychotherapeutic Medicine. Edited by Helen Leland Witmer, Ph.D. An Experimental Course for General Physicians Given by Walter Bauer, M.D., and others. Introductory Chapter by Geddes Smith. Cloth. Price, $3.75. Pp. 464, with 5 illustrations. The Commonwealth Fund, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, 1947.

This book is a compilation of the recorded verbatim discussions between a group of general practitioners, seven psychiatrists and two internists during a two week course of study. There is, first, a lecture, then actual case presentation followed by an exchange of information based on the personal experience of the authors. These discussions make the book especially valuable to any physician, specialist or general practitioner who encounters these same problems in his daily practice. This is one of the few books on psychosomatic medicine which actually are concerned with the heart of the problem; namely, how to handle a patient with psychogenic complaints. Most of the current publications are so bogged down with confusing terminology, broad generalizations and lengthy verbiage that the average intelligent physician can find little information in them to help him in the actual treatment of the patient. This book will make the physician more secure in the handling of patients with psychogenic complaints.

Exercise During Convalescence: A Manual of Adapted Exercises. By George T. Stafford, Ed.D., Professor of Physical Education, University of Illinois, Urbana, Ill. Cloth. Price, $4. Pp. 281, with 36 illustrations. Drawings by William S. Pusey. A. S. Barnes & Co., Inc., 67 W. 44th St., New York 18, 1947.

This book is written particularly for those engaged in rehabilitation work in the armed services. Physiatrists and physical and corrective therapists will find many helpful suggestions in planning their convalescent programs. The author is well qualified by his many years of experience in physical education. The book contains thirteen chapters. Dr. Stafford states that all programs, such as he outlines, must be carefully supervised by a physician and by one well trained in physical medicine. Physical educators with an excellent knowledge of kinesiology are qualified to give a general exercise program. Caution, however, must be used with regard to general and especially specific exercise programs in civilian hospitals, which do not have many strong, young men patients who can take a convalescent program as outlined in the book. Many are either too young or too old, and many have conditions which require an accurate program of muscle reeducation. The average physical educator usually has had no specific training in muscle reeducation. Corrective gymnastics are often thought to include this, but they actually do not, since corrective gymnastic exercises are meant to cover large muscle groups usually and not to require specific attention to true muscle reeducation or to the orientation of specific muscles. Therefore it is inadvisable to have physical educators treat the sick and handicapped except to give exercises for the uninvolved parts or conditioning exercises to nearly normal patients. With these cautions in mind, this book offers real help toward hastening the patient's recovery by exercise during convalescence.

Operative Oral Surgery. By Leo Winter, D.D.S., M.D., F.A.C.D., Professor of Oral Surgery, New York University, New York. Third edition. Cloth. Price, $12.50. Pp. 1167, with 1240 illustrations. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1947.

This is a good textbook for students. The diagrams and drawings on the chapter of local anesthesia are most explicit and instructive. Under general anesthesia, the various drugs, technics, difficulties in their use and, above all, the value of preanesthetic medication are well described. The section on chemotherapy brings the student up to date. The chapter on exodontia is profusely and well illustrated, but the author has a tendency to refer wrongly to all unerupted teeth as impacted teeth. Surgical technic of the removal of teeth is described and illustrated in detail.

A large section of this book is devoted to tumors. The author includes and describes the operation known as apicectomy under "cysts of the jaws." This procedure is done only under certain conditions such as when there are nonvital teeth with periapical infection. Photographs, diagrams, and roentgenograms are numerous and enhance the excellent description in the text. In the discussion of adamantinomas, it would probably be better from a teaching standpoint to

discuss the etiology before the symptomology. There are two schools of thought on the operation referred to as alveolectomy; namely, that it should be immediate and that it should be delayed. The latter is not discussed at all. The author suggests consultation with the rhinologist in fractures of the maxilla where there is nasal and antral involvement. The trend is to refer such cases to men capable of handling extensive fractures of the face rather than to divide responsibility unnecesarily.

The first Gilmer method of intermaxillary wiring for mandibular fractures is no longer used, except possibly as a temporary emergency measure, to be substituted later. In mandibular fractures, the author has a tendency to advise general anesthesia for reduction. Most men in this work use local anesthesia or sedatives alone. The use of general anesthesia is the exception rather than the rule. For clarity and continuity, the immediate treatment of the injured patient should be discussed before the mechanical treatment of the fractured jaws rather than after.

The chapter on diseases and disturbances of the temporal mandibular joint is a most welcome addition to the literature.

Laboratory Technique in Biology and Medicine. By E. V. Cowdry, Professor of Anatomy, Washington University, St. Louis. Second edition. Fabrikoid. Price, $4. Pp. 269. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, 1948.

The title of this book, which has been changed from "Microscopic Technique" in the first edition, is misleading, for the book still deals almost entirely with microscopic technics and expositions of microscopic findings. After brief chapters on choice of methods of biologic study and on standardization of stains, the book is essentially an encyclopedic dictionary of biologic terms and technics. The subjects are arranged in alphabetical order and the expositions vary in length from 1 line to 11 columns. Many of the long articles are by guest authors, as for example "Oxidation-Reduction Potential," by C. Carruthers, and "Quartz Rod Technique," by M. H. Knisely. The chief value of the book is as an introductory reference to laboratory phases of biology. It will be of most value to the young research worker in any field of histology. To the experienced histologist, descriptions of the technics, though brief, have enough detailed information to serve as a good laboratory reference book.

Clinical Endocrinology and Constitutional Medicine. By A. P. Cawadias, O.B.E., M.D., F.R.C.P., Endocrinologist to the Order of St. John Clinic, London. Fabrikoid. Price, 42s. Pp. 368, with illustrations. Frederick Muller, Ltd., 29 Great James St., London, W. C. 1, 1947.

In the preface the author regrets that the late Sir Thomas Lewis "unfortunately over-emphasized the physiopathological chapter of diseases and under-rated the great importance of clinical observation." He then presents over 300 pages of unscientific nonsense and modestly (sic) concludes "I have developed the modern constitutional point of view on medicine" (page 359). In the treatment of goiter he says, "I prefer the homeopathic dilution (6 times) as the dangers of aggravation through iodine, and of production of a toxic goitre, are very real" (page 82). American physicians will be surprised to find that in the treatment of Graves' disease "protein restriction is indicated because proteins raise metabolism and tire the liver" (page 99). The author has seen good results from "galvanisation or galvano-faradisation of the thyroid." In the treatment of myxedema he advises, as an adjuvant to thyroid, the use of sulfur. On page 100 he states, "It is a powerful oxidiser, and can be used either in colloidal form, as an absorbable organic preparation, or in homeopathic form."

In regard to the treatment of diabetes he writes, "Spa treatment is of the greatest importance and except in very severe cases should always be prescribed. Choice of spa is based on the special features of various mineral waters. According to individual features, Vichy, Vittel, La Bourboule, Harragate or Bath is selected. High altitude health resorts, particularly those of the Engadine, often prove far more beneficial than spas."

The author makes the statement that, in the treatment of diabetic acidosis, "An enema or aperient is necessary for elimination of poisons" (page 314).

Headings which are intriguing are used, such as The Postpuberal Hypotestosteronic Eunuchoid, Cerebropituitary Hyperoestrinic Metrorrhagia, Hypotestosteronic Morpho-Psychological Androgynoidism, Cerebro-Pancreatic Hyperinsulinic Hypoglycaemia.

This is just about the worst book on endocrinology the reviewer has ever seen. It is incredible that, when the school children in England are deprived of textbooks because of a shortage of paper, so much should have been wasted in this book. Few American physicians will wish to aid in the depletion of England's supply of paper by purchasing this book. Most will continue to be grateful to Sir Thomas Lewis for his contributions to science and medicine.

Pharmacology and Therapeutics in Nursing. By Marion Sylvester Dooley, A.B., M.D., and Josephine Rappaport, R.N., B.S., Assistant Chief, Nursing Education, Veterans Administration Hospital, Alexandria, Louisiana. Cloth. Price, $3.75. Pp. 444, with 26 illustrations. McGraw-Hill Book Co., Inc., 330 W. 42nd St., New York 18, 1948.

This new textbook has an entirely new approach to the problem and should be useful for the nurse. The nursing care is emphasized. It is increasingly important for the nurse to be familiar with the drugs, particularly the new ones. As the authors state, "by concentrating the discussion on standard drugs and using the metric system throughout, it saves priceless hours."

There are only a few criticisms. On page 91 under the anticonvulsants no mention is made of trimethadione ("tridione"). On page 159 "mecholyl chloride" and "mecholyl bromide," which has a much wider use, are not mentioned at all. On page 162 appears the statement, "taking it to 'reduce' is also a dangerous delusion." This, of course, is not true. There have been many reports of the usefulness of amphetamine sulfate ("benzedrine sulfate") in the diet program for weight reduction. On page 318 the use of gentian violet is mentioned for the treatment of pinworms. However, it is important to mention that treatment with gentian violet must be continued for three alternate weeks in order to be effective. The greatest number of failures is due to the fact that gentian violet is not given in a large enough dose or for a long enough period of time.

Physical Education: Interpretations and Objectives. By Jay B. Nash, Ph.D., Chairman of the Department of Physical Education and Health, School of Education, New York University, New York. Cloth. Price, $3. Pp. 288, with illustrations. A. S. Barnes & Co., Inc., 67 W. 44th St., New York 18, 1948.

In this little volume the author attempts "to investigate the place of education in a democracy; to indicate the specific contributions of physical education to general educational objectives; to indicate the relationships between physical education as a teaching subject and democratic outcomes in terms of health, recreation and citizenship."

Part I does a good job of defining physical education and showing its important place in the educative process. It is marred by a minor inaccuracy on page 42, where the author states that the one crop pattern of farming through diminishing the mineral resources of the soil is "a predisposing factor of rickets for millions of people."

Part III is introduced by a baffling figure showing the four level development in education in man. Over the figure is the cryptic title "Organismic Whole Gestalt of Emergents." On the next page the author falls into the error of defining immunity only in the limited terms of phagocyte proliferation. But in spite of this inauspicious beginning, part III is perhaps the most valuable part of the book because of its elucidation of organic, neuromuscular, interpretive (cortical) and emotional development.

In part IV, the author discusses recreation, health and character as objectives of physical education; it is a pleasure to note his broadmindedness in such statements as the following: "Physical education has had no monopoly on the setting up of or the contributions to recreational standards. This has been the responsibility of all education and of the total community. A special tribute should be paid to science, vocational education, music and the languages." "Physical education has no monopoly on contributions to the health of the human organism. As a matter of fact, in comparison with all the other educational and community factors, its contributions are relatively small. The very name, Department of Health and Physical Education, carries some unfortunate connotations. One of them is that health and physical education are synonymous or, even worse,

that physical education departments should take over the responsibility for the health of the school-age child. Both of these ideas are very unfortunate."

Though this volume is written primarily for use as a text for students majoring in physical education, it should hold interest for school administrators, school physicians, health educators, recreation leaders and parents.

Myotonia: Thomsen's Disease (Myotonia Congenita), Paramyotonia, and Dystrophia Myotonica: A Clinical and Heredobiologic Investigation. By Eivind Thomasen. Translated from Danish by Finn Brink Carlsen. Denne Afhandling er af det lægevidenskabelige Fakultet antaget til offentlig at forsvares for den medicinske Doktorgrad, København. Paper. Pp. 251, with illustrations. Universitetsforlaget i Aarhus, Aarhus, Denmark, 1948.

This excellent review and report of new cases of myotonia comes from the hospitals and scientific departments associated with the University of Copenhagen and from the Institute for Human Genetics in Denmark. The translation from Danish into English, although a little stilted, is so good that the author's meaning is seldom unclear. The various forms of myotonia are fully delineated, the text being supplemented by pertinent illustrations, an adequate bibliography and case reports of twenty families. The book only lacks an index to make it a completely useful monograph on two syndromes of muscular disability. To Thomsen's original concept of myotonia congenita, first described from his own symptoms in 1876, has been added a subvariety, paramyotonia. Dystrophia myotonica, which the author feels is a different disease, also has myotonia as one of its symptoms. Myotonia acquisita, a nonhereditary type of myotonia, does not, in Thomasen's opinion, have sufficient basis for differentiation as a special group. Myotonia congenita, on the other hand, shows dominant heredity, with varying manifestations. The author gives a brief biography of Dr. Thomsen and traces additional cases in his family from persons now living in Denmark. Myotonia disappears with heavy doses of quinine, a drug of some use in the treatment of Thomsen's disease, but less valuable in cases of dystrophia myotonica. Thomasen found that most patients with myotonia were made worse by cold, fatigue, menstruation and pregnancy. Fright may bring on an acute attack. The disease tends to become less burdensome in old age. These conclusions, and others of equal value, carefully compiled by the author, give the book an outstanding position in the literature of muscular diseases.

Intracranial Tumors. By Percival Bailey, Professor of Neurology and Neurological Surgery, University of Illinois, Chicago. Second edition. Cloth. Price, $10.50. Pp. 478, with 171 illustrations. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Illinois, 1948.

This admirable book has evidently been very popular, for a second edition has had to be brought out. In the preface to this edition, the author states that "errors have been corrected and recent advances in our knowledge inserted," but this reviewer, with the first edition alongside of the second, has found few changes.

The two important advances in neurologic surgical diagnosis that have been made since the first edition appeared are angiography and electroencephalography. On the first of these, the author comments briefly (page 395); he expresses the hope of being able by this method to detect glioblastomas and other types of tumors before operation. About electroencephalography, however, he does not comment at all; at least, this reviewer has been unable to find a reference either in the text or in the index, though there is one reference to the subject (no. 226) in the bibliography. Yet it would have been of real interest to have had the author's opinion about this method of examination and his estimate of its value.

There are a few inconsistencies that are rather striking. In his preface, the author says that localization of tumors has been solved by the introduction of ventriculography; yet on page 395 he states that he makes use of it in only 15 per cent of his cases. This is not in accord with usage now customary in most neurosurgical clinics. The difficulty the author describes in diagnosing tumors of the third ventricle might be somewhat obviated if air were injected in one side only, and then roentgenograms taken before air is injected on the second side.

Because of the author's objection to glazed paper, it was not possible, in either edition, to reproduce roentgenograms. Therefore drawings of roentgenograms were made which, to many readers, are unsatisfactory. For the same reason, drawings of patients were used instead of much more satisfactory photographs. Hence, in the new edition, both reviewer and reader will undoubtedly welcome the inclusion of an atlas of sixteen roentgenograms which are well reproduced. If only there had been more!

The criticisms expressed in this brief review in no way detract from the great value and importance of this work. The author is one of the leading authorities on the pathology of brain tumors, and the subject is approached primarily from that angle. His views throughout are sound and based on vast experience. This book should be in the library of every neurologic surgeon. Furthermore, it is so clear and so readable that all medical students would do well to study it.

The Engaged Couple Has a Right to Know: A Modern Guide to Happy Marriage. By Abner I. Weisman, M.D., Assistant Visiting Gynecologist and Obstetrician, Metropolitan Hospital, New York. Foreword by Dr. Abraham Stone. Cloth. Price, $3. Pp. 256, with 14 illustrations. Renbayle House, 1165 Broadway, New York 1, 1948.

The past few years have brought out many much needed books for engaged couples and those needing help in marriage adjustment. This book deserves to be high on the list of recommended books in this field. It is most inclusive without being too lengthy. It touches on marriage historically, as well as giving it place in present day society. It discusses readiness for marriage and how to select a mate. It takes up health and physiology and the role of sexuality in a frank and capable manner. It also goes into the matter of blood incompatibility and sterility, a field in which the author is already an authority. It discusses the honeymoon and sexual adjustment and even includes the advent of the first baby, as well as the various facets of planned parenthood. There is a forward by Dr. Abraham Stone and a fairly lengthy list of suggested reading for young persons contemplating marriage. The author is a gynecologist who has already written for the medical profession and the laiety. It is a welcome phenomenon to see a book so sensitive to the emotional and social problems within medical practice come from one within a speciality other than psychiatry.

Die Bildung des Arztes: Ein Beitrag zur Bildung des Menschen überhaupt. Von Curt Oehme. Paper. Pp. 39. F. H. Kerle Verlag, Theaterstrasse 18, Heidelberg, 17a, 1948.

This is an interesting monograph comprising a series of lectures presented at the University of Heidelberg on the problems of general and professional education facing Germany today.

The roots of the present depression in medical education can be traced as far back as the first World War, as shown by the comparatively few contributions to medical knowledge published in German periodicals since that time.

Social economic conditions, the Nazi-autocratic restriction of scientific interchange with other countries, have interfered with medical progress as compared with England and America. Racial prejudice and war psychoses have been a further factor, and the story of the Nuremberg trials distinctly reflected the low plane to which the greatness of German medicine had fallen.

The present chaotic state of German medical education is ascribed to four causes: (1) the lowering of premedical educational standards, the mass admission of large numbers of students poorly prepared for the study of medicine and inadequate teaching facilities in the several university medical schools; (2) an attitude of arrogant self satisfaction with the existing educational system; (3) loss to medical faculties of the great leaders of a former day; replacements can only be made from younger physicians inadequately prepared for medical teaching; (4) teaching at the bedside and careful laboratory training are practically nonexistent, while the spirit of research is hardly evident anywhere.

The author maintains that a revival of medical education in Germany implies a complete revision of the entire educational system, and above all a reawakening of the spirit and soul of

medicine. A generation will pass before the results of the teaching of a sound philosophy of living will be evident. The author makes the plea for a more humanistic approach to the study of medicine, coupled with a more complete preparation for the study of the basic and clinical medical sciences with a keen appreciation of their spiritual and cultural values in the art and practice of medicine.

Such, according to the author, is the challenge that confronts medical education in Germany today.

Public Health Administration in the United States. By Wilson G. Smillie, A.B., M.D., Dr.P.H., Professor of Public Health and Preventive Medicine, Cornell University Medical College, New York. Third edition. Cloth. Price, $6.50. Pp. 637, with 43 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1947.

This splendid textbook, first printed in 1935, is now in the third edition and has been thoroughly revised. It is well indexed, nicely arranged, rather well illustrated, particularly with graphs, and in general gives an attractive appearance. Part I has to do with organizations in the United States. Part II has for its subject "The Administrative Control of Communicable Diseases"; part III, "Basic Activities of a Health Organization," and part IV, "Organization of Public Health Programs."

The book is subdivided in such a way that it will be easily used as a textbook and has evidently been arranged with that in mind. Particularly suitable would be the use of this book by junior or senior medical students. It is well documented at the end of the chapters.

Dr. Smillie has done a notable work in preparing this book and keeping it up to date. It can be recommended without reservation.

A Handbook for Dissectors. By J. C. Boileau Grant, Professor and Director of the Department of Anatomy, University of Toronto, Toronto, and H. A. Cates, Professor of Anatomy, University of Toronto. Third edition. Cloth. Price, $3. Pp. 415, with 19 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

This excellent little book is of especial value to medical students at this time. The third edition is the product not only of many years sound teaching, but also of eight years' experience with the earlier editions. The first edition referred to the authors' textbook only; this one does not refer to any single textbook but can be used with equal convenience with any or all of them. Its outlook is clinical—preparation for medicine and surgery. Sound knowledge of gross human anatomy is obviously a basic essential of such preparation. Dissection is rightfully required by all the state laws. But biochemistry, bacteriology, pharmacology, etc., are also fundamental and must have places in the preclinical medical curriculum. The time available for dissection is reduced, and therefore cannot be wasted but must be spent to the greatest advantage. On this consideration the Canadian book is admirable. On completing one careful dissection with its guidance, medical students *can* go on with the medical curriculum. But most medical students are also students of general biology and specialists in some field. They cannot be content with the minimum study of gross human anatomy. They will return to it many times, often with further dissection.

Your Skin and Its Care. By Howard T. Behrman, M.D., and Oscar L. Levin, M.D. Cloth. Price, $2.50. Pp. 255, with illustrations. Emerson Books, Inc., 251 W. 19th St., New York 11, 1948.

This book is intended for the lay reader, although it contains information which is presented in such a way that it makes interesting reading for others who wish orientation concerning knowledge of the skin. Fourteen chapters provide discussions on the structure of the skin and its function, the relation of health to the skin, care of the face, quackery, diseases of the skin, care of the hair and other problems of similar nature. The book is not too technical for those who have a genuine interest in their skin problems, although of course it is not intended as a textbook for medical students or others who have need for specialized training. It is the type of book to which the physician can refer his patients who want more information than can be obtained during the average consultation session.

Diseases of the Eye. By Sir John Herbert Parsons, C.B.E., D.Sc., F.R.C.S., Consulting Ophthalmic Surgeon, University College Hospital, London, and Sir Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Surgeon Oculist to the King. Eleventh edition. Fabrikoid. Price, $7. Pp. 732, with 389 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1948.

The eleventh edition of this popular short textbook has been revised to include therapy with penicillin and sulfonamide drugs and short descriptions of toxoplasmosis and brucellosis. There are included chapters on causes and prevention of blindness, hygiene of vision, outline for complete examination of the eyes and therapeutic notes giving strength and dosage of drugs used in ophthalmology. The final 14 pages give the visual requirements of Great Britain for the army, navy, air forces, civil aviation, merchant marine, railroad workers, civil employees, police force and drivers' license.

The book is an adequate short textbook in ophthalmology for students and general practitioners.

Sport und Kreislauf. Sammlung der Referate gehalten am IV. Sportärztlichen Zentralkurs 1946 in Lausanne. Herausgegeben durch den Schweizerischen Landesverband für Leibesübungen und die Verbindung der Schweizer Ärtze. Mit Unterstützung der Firma Dr. A. Wander A. G., Bern. Paper. Price, 12.80 Swiss francs. Pp. 154, with 21 illustrations. Hans Huber, Marktgasse 9, Bern, 16, 1947.

This little volume is a compilation of the reports made on the heart and circulation at the 1946 Sports Physicians' Conference held at Lausanne, Switzerland. Previous to World War II, a good deal was heard about the European sports physicians and the interest abroad in study and research on the physiologic results of sports activity. Evidently in postwar years there is renewed interest among physicians in this subject. Included in the symposium are papers on functions of the heart and circulation in reference to participation in sports, cardiologic considerations in sports medicine, electrocardiographic changes in connection with continued physical effort, ergometric and spirometric measurement of reaction to exercise, suggestions on the examination of school children and a supplement on research in sports medicine.

The Treatment of Impotence with Special Reference to Mechanotherapy. By Joseph Loewenstein, M. D. Foreword by Eric B. Strauss, D.M., F.R.C.P., Physician for Psychological Medicine, St. Bartholomew's Hospital, London. Cloth. Price, 6s. Pp. 49, with 4 illustrations. Hamish Hamilton, Ltd., 90 Great Russell St., London, W.C.1, 1947.

This short monograph deals primarily with mechanotherapy in the treatment of impotence. The author gives a history of the various apparatuses that have been used in the treatment of impotence, and then describes in detail a gadget called the "coitus training apparatus." Then follows a discussion of indications and technic of its use. Eleven case reports of impotence treated by this method combined with psychotherapy are given. It is difficult to evaluate this method of treatment. Apparently, from the evidence presented, the gadget described by the author has a place in the treatment of some forms of impotence. This monograph will be of greatest interest to those who specialize in sex disorders.

An Index of Modern Remedies. By William Mair, F.R.S.E., F.C.S., M.P.S. For the Medical and Pharmaceutical Professions Only. Fourth series. Paper. Price, 3s. Pp. 68. The Scottish Chemist, 240 Albert Drive, Pollokshields, Glasgow, S.1, 1948.

This brief index of remedies is concerned primarily with the agents that are available in the British Isles, and for this reason the booklet will provide a source of information to those that are interested in the nomenclature and composition of British remedies. It is not, of course, a therapeutic guide. The booklet will be of interest primarily to the teacher, librarian and those who occasionally have reason to interpret prescriptions from Great Britain.

Tabulae biologicae. Editores: G. Backman, et al. Vol. XXII Pars I.: Oculus. Editores: K. Steindorff, E. P. Fischer, J. S. Friedenwald et Arnold Sorsby. Paper. Pp. 408, with illustrations. Uitgeverij Dr. W. Junk, N. Z. Voorburgwal 64, Amsterdam (C), 1947.

This paper-covered book, which is part I of volume XXII, is concerned with the eye. In part it is a tribute to Kurt Steindorff, who was one of the early students of the eye. Chapter by chapter pertinent information concerning this organ is presented, so that those with various interests—biologist, chemist or surgeon—will find interesting data.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

NITRITOID REACTION

To the Editor:—**Nitritoid reactions are not supposed to occur with oxophenarsine hydrochloride. Please give an opinion on the following reaction and suggestions for future management. The patient is a white woman aged 19 years. Except for secondary syphilis when the patient was first seen, physical examination was completely negative. History of exposure or contact is lacking, so that the date of the primary lesion is unknown. The treatment followed was that recommended by the Cooperative Clinical Group for early syphilis. During the initial part of this schedule, she also received 8,500,000 units of pencillin. Until two weeks before I first saw her reactions were absent except for occasional moderately severe nausea beginning an hour or two after the administration of the oxophenarsine. These cleared completely on the following morning. Reactions did not occur during the bismuth phase. Then, within five minutes of an injection of freshly prepared oxophenarsine, her face became slightly flushed, she complained of lightheadedness, appeared anxious and suddenly fainted. The pulse was extremely weak, and respiration was shallow. She responded to epinephrine, but was weak and had nausea with retching for a half hour after she recovered from the faint. Nausea persisted for several hours, until she fell asleep for the night. This reaction occurred on the fourth injection in the second oxophenarsine series. To be certain that it was not partly of psychic origin, I gave her an injection of sterile water the next time and reaction did not occur. She is now receiving bismuth compound again and there have been no more reactions. Is it advisable to continue the oxophenarsine when it is time to start it again and have her take ephedrine the day before and after the injection, or use some epinephrine preceding the injection? Is it better to use a different arsenical, or eliminate use of arsenicals entirely?**

M.D., Pennsylvania.

ANSWER.—The question whether this 19 year old female patient with secondary syphilis requires any therapy with arsenic or bismuth compounds depends on when she received the 8,500,000 units of penicillin and how it was given. If this amount of penicillin was administered early in the patient's treatment, and given every two or three hours day and night in aqueous solution within a period of four to fifteen days, or if, alternatively, it was given by daily intramuscular injections of penicillin in an absorption-delaying medium, such as peanut oil–beeswax or procaine penicillin, over a period of ten days or more, little if anything is to be gained by giving her arsenic and bismuth compounds. The chance of improving on the results of this amount of penicillin alone are relatively small and the risks of treatment greatly increased.

Eight and one half million units of penicillin given for secondary syphilis will provide a 10 to 20 per cent failure rate at the end of eighteen to twenty-four months. Conversely, it will provide an 80 to 90 per cent chance of "cure" without the addition of arsenical therapy. The consensus, as expressed in the report of the Syphilis Study Section to the Council on Pharmacy and Chemistry, "Penicillin in the Treatment of Syphilis" (J. A. M. A. **136**:873 [Mar. 27] 1948), is that penicillin should be used alone as an initial course of treatment for early syphilis. Arsenic and bismuth compounds, if employed at all, should only be used as retreatment combined with penicillin in the event of failure of the first course of treatment.

It is suggested that in this patient treatment now be stopped and that she be followed at monthly intervals with physical and quantitatively titered serologic recheck examinations. If her progress is satisfactory at the end of one year, these recheck examinations may be carried out every three months during the second year and every six months thereafter. The patient's spinal fluid should be tested about six months after the initiation of treatment and again at the end of the second year of observation.

Nitritoid reactions do occur from oxyphenarsine hydrochloride ("mapharsen"), though they are much less frequent than after the arsphenamine series of drugs. If it becomes necessary to use arsenic in this patient again, oxophenarsine should be cautiously employed, beginning with small doses, e. g., 10 mg., and gradually increasing.

ADOPTION

To the Editor:—**A couple has made application to a welfare agency to adopt a child. The welfare worker asked them how they would feel about adopting a child under the following conditions. The father and the mother of the child are university graduates. The father is known to have had a positive Wassermann reaction. The mother's Wassermann reaction has always been negative. Examination of cord blood at the time of the birth of the child showed positive reaction. However, repeated Wassermann tests on the child and mother after delivery have elicited negative reactions. No history as to kind or type of treatment either of father or mother was obtainable. This couple wants to know whether there is any chance of the development of congenital syphilis in the child or whether it is likely that any congenital deformity or weakness could show up from this condition in later life. I have been asked to give an opinion on this matter before they consent to adopt the child.**

M.D., Arizona.

ANSWER.—It is difficult to give a specific answer to the inquiry because the age of the child to be adopted is not given. The fact that examination of cord blood at the time of the child's birth gave positive results does not indicate that the child does have or will have congenital syphilis, because that serologic test is of the mother and not of the child. The question whether or not congenital syphilis will develop depends not on whether the antigen went over into its blood stream, but on whether the Treponema pallidum did. If the antigen alone, and not the T. pallidum, went through to the child's blood, the reaction to the child's serologic test usually will become negative within a period of approximately four months. Accordingly if the child to be adopted is more than 6 months old, if it has had repeated serologic tests with negative results since a month or so after birth, and if the child manifests no signs of congenital syphilis, the probabilities are that evidence of the disease will never develop. It would be advisable, however, to have the child examined by a pediatrician interested in syphilis or a syphilologist before approval is given to adoption of the child.

SYPHILIS IN PREGNANCY

To the Editor:—**A woman is now pregnant for the fourth time in eleven years. About three years prior to her first pregnancy, a 4 plus Wassermann reaction was obtained in the course of a routine examination. The only history obtainable relative to syphilis was that old medical records revealed that her mother had died of aortic heart disease and had also had a 4 plus Wassermann reaction. Older and younger siblings were examined repeatedly and found to have negative serologic reactions. While this patient did not show stigmas of syphilis, and did not give any history suggestive of primary or secondary lesions, she was given a full course of treatment with oxophenarsen hydrochloride and bismuth compound. She was again treated similarly during each of her previous pregnancies, giving birth to normal children without physical or serologic evidence of syphilis. In spite of the extensive treatment and child bearing, the patient continues to have a 4 plus serologic reaction. Should she be treated again during this pregnancy? If she is to be treated, can penicillin be substituted for arsenicals, which the patient dreads because of the unpleasant minor side reactions which have accompanied these injections? If penicillin is to be used, what dosage do you recommend for ambulatory treatment with penicillin in oil and wax or the newer procaine penicillin preparations? What is the optimum time to treat the patient?**

Fred S. Taber, M.D., New Brunswick, N. J.

ANSWER.—A woman with congenital syphilis runs virtually no risk of passing the disease to her unborn child, even though untreated. Since the evidence of congenital infection of the mother in the present instance is inconclusive, however, it must be assumed that her disease is acquired. The syphilis status of the woman's husband is not mentioned. If he has not been examined it might be worth while to do so, since a positive blood serologic reaction or other evidence of the disease would make the possibility of an acquired infection in this woman more likely.

A woman who has had adequate treatment with arsenical and bismuth compound for syphilis and who has responded normally runs virtually no risk of giving birth to a diseased infant, even though untreated during her pregnancy. Cole and the cooperative clinical group in their article, "Syphilis in Pregnancy" (*Ven. Dis. Inf.* **15**:83 [March] 1934) found that among 52 women considered "cured" there had been no evidence of a syphilitic child's having resulted from pregnancies up to fifteen years after infection. The usual advice, however, was to treat in each subsequent pregnancy because of the difficulty of determining "cure." When the disease is of long standing and normal children have resulted as a result of previous therapy the possibility of infection of the fetus becomes even less. Only occasionally does an infected fetus result when the disease in the mother is more than ten years old.

The one disconcerting point in the present case is that the expectant mother is seropositive. Nothing is said of study of the spinal fluid. If this has not been performed it should be done (cell count, total protein, serologic test for syphilis and colloidal test). A good time to carry this out would be during the hospitalization immediately after delivery. A seropositive

mother is more apt to have some remaining activity of her infection than a seronegative one, and the risk of an infected fetus if untreated is appreciably greater.

Since penicillin therapy entails so little likelihood of reaction, is so effective in preventing congenital syphilis and is so easily given over a relatively short period, it would probably be wisest to treat such a patient with this drug even though the risk of infection of the fetus without treatment is small. Treatment with penicillin may be given at any time in the pregnancy, preferably before the sixteenth week, but it is effective even in the last month. Six hundred thousand units of penicillin in oil and wax, and presumably similar dosage of procaine penicillin, given once daily intramuscularly for eight days for a total dose of 4,800,000 units, is sufficient. Some workers prefer larger total dose, for example 6,000,000 units in ten days or even more than this, but evidence is lacking that this is necessary to protect the fetus. Only one course need be used and no adjunct chemotherapy with heavy metal compound is indicated. Results of such therapy are described in "Treatment of the Syphilitic Pregnant Woman with Penicillin in Oil Beeswax: A Comparison with Results Obtained Using Aqueous Sodium Penicillin" by N. R. Ingraham Jr., E. K. Rose, H. Beerman and others (*J. Ven. Dis. Inform.* **28**:155 [Aug.] 1947).

It is customary after such treatment to perform a quantitative titered serologic test for syphilis once monthly until term to determine the serologic response and to watch for evidence of serologic relapse. In a seroresistant case such as has been described, however, serologic response to penicillin therapy, other than the fluctuations which normally occur in repeated studies of seroresistant cases, is not to be expected. Treatment, therefore, must be empiric, based on experience with other patients, and serologic follow-up, while of academic interest, will not form a real guide as to the future handling of the mother. It is well to bear in mind that if the mother is seropositive at delivery the infant may also be seropositive though not syphilitic. The serologic follow-up of such an infant is described in any of the recently published standard texts for syphilis.

ERYTHROBLASTOSIS

To the Editor:—**A 36 year old white woman is Rh negative and slightly less than two months pregnant. Her husband is homozygous Rh positive. They have 3 living children, the youngest being 10 months of age and the only one of twins born of the last pregnancy to survive. The other twin died soon after receiving 60 cc. of Rh-positive blood when 2 days old. The living twin withstood the same type of transfusion although she did have an epistaxis. The antibody titration, post partum, was 1/32, and a recent test showed the same concentration of antibodies. Since the father is homozygous positive this present pregnancy is certain to result in an Rh-positive baby and therefore a recurrence of erythroblastosis. Are these circumstances a justifiable reason for a therapeutic abortion? If not, is there any method of preventing the development of further antibodies in the mother to endanger the baby? Would induction of labor, or cesarean section, before term increase the chances of the baby? My present plans are to terminate the pregnancy about two weeks before term by induction of labor or cesarean section, depending on the condition of the cervix at that time, and give the baby an exsanguination transfusion of 350 cc. of Rh-negative blood devoid of antibodies through the umbilical vein. Will you please offer any further suggestions or criticisms?** T. A. Strang, M.D., Long Beach, Calif.

ANSWER.—The query does not furnish information on several points which could help in formulating a more complete answer: 1. What manifestations of fetal erythroblastosis were present in the deceased twin? In the surviving twin? 2. The reference to the antibodies does not state what type of Rh antibody was present. Recent studies have shown that blocking antibodies have a more ominous prognostic significance than agglutinins. On the basis of the information contained in the query the following answer is offered.

There is no justifiable reason for a therapeutic abortion. Modern methods of treatment, especially replacement transfusion, offer an excellent outlook for saving the majority of infants with fetal erythroblastosis, except those with universal fetal hydrops.

Methods are not available at present to prevent development of further antibodies in the mother.

Opinions of experts are divided on the question of advisability of terminating pregnancy by inducing labor or by cesarian section. It may be that further experience with replacement transfusions will encourage such procedure.

The plan offered in the query is reasonable, but it may be still better to test for Rh antibodies (agglutinins, conglutinins and blocking antibodies) at frequent intervals during pregnancy. Observation of the curve of the various antibodies may be helpful in anticipating the degree of dosage to the baby, and it may help in selecting the time for the operation.

The replacement transfusion should be given only if there are indications for it: evidence of disease, or Rh-positive blood in the newborn infant. The latter must be expected in view of the fact that the father is homozygous Rh positive. In spite of that expectation the baby's blood should be Rh tested immediately after birth.

It is probably better to give no less than 500 cc. as replacement transfusion and to withdraw a similar amount minus about 10 cc. per pound of the infant's weight.

IMMUNIZATION AND LEUKEMIA

To the Editor:—**A recent scare has come about in this region about a possible relation between immunizing doses of diphtheria, pertussis and tetanus toxoids and leukemia, especially in children of school age. If there has been anything in the literature I have missed it. At least one nearby physician, I understand, has stopped administering such toxoids, and the rumor has reach such proportion that I would appreciate an authoritative statement.** M.D., Minnesota.

ANSWER.—Evidence is not available of any relation between diphtheria, pertussis and tetanus immunizing agents and leukemia. Immunization procedures might be instituted against the diseases mentioned, and some time later the discovery made that the child had a preexisting blood dyscrasia. However, Byers and Moll (*Pediat.* **1**:437 [April] 1948) have reported instances of encephalitis following pertussis vaccine injections. Toomey discussed the latter subject at the recent meeting of the American Medical Association June 23, 1948. Except on rare occasions, such as exposure to smallpox, inoculations for the purpose of active immunization are, as a rule, better postponed if the subject is not in good health.

BLEEDING GUMS

To the Editor:—**What is recent opinion on causes and treatment of pyorrhea? A married woman aged 36, otherwise in excellent health, has had slightly bleeding gums for years. She has been informed that there is deep pocket formation and loss of alveolar bone around all her teeth, probably due to pyorrhea. She has taken excellent care of her teeth, and had a well balanced diet, including plenty of milk, fresh fruits and vegetables. Basal metabolism and blood chemistry tests are normal. She does have some malocclusion. Periodontists advise the extraction of the most severely involved teeth (though they differ as to how many have to be removed) and claim that they can treat the remaining teeth and arrest the pyorrhea and thus the alveolar destruction. Other dentists are more skeptical of the outcome of periodontal treatment. The patient is particularly concerned about the cause of the gum disturbance because her daugter, aged 9, who has been carefully watched as to mouth hygiene, diet and vitamin intake, has recently shown evidence of bleeding gums. Is such a tendency inherited? Both mother and child have always been underweight.** M.D., New York.

ANSWER.—The causes of periodontal lesions may be classified for the most part in three categories; i. e., (1) dysfunctional, (2) irritative and (3) systemic or idiopathic, with the possibility of any combination of them. Under these headings may be grouped many individual factors, the principal half dozen of which, in order of importance, are traumatogenic occlusion, poor hygiene, calculus, dietary deficiency, poor restorative dentistry and systemic causation.

On the accurate diagnosis of the etiologic factor or factors will depend the rationale of successful therapy. Starting with the three categories, all the teeth and their supporting structures must be placed in a state of equilibrium in which no tooth or its peridontium is subjected to stresses beyond its physiologic limits during normal masticatory functions. In this regard, the eradication of traumatogenic occlusion is of prime importance. In dealing with the second category, a program must be carried out to bring about the remission of all agencies contributing to inflammatory processes. The third and final category with systemic disturbances includes those conditions which might adversely alter the body metabolism. Failure to recognize some one active causative process may be sufficient to retard or completely forestall a satisfactory prognosis.

The brief history of the case mentioned does not permit a specific answer. It would suggest that the active causes may be both dysfunctional and inflammatory because of the known malocclusion and gingival hemorrhage. The normal basal metabolic rate and hematologic findings point toward a local origin. As to whether a number of teeth need extraction or not, it could only be decided by direct examination of the patient.

The role played by heredity in such cases might obtain only after all the commoner factors have been ruled out. In the child's case, if the oral hygiene is really good, a tentative suggestion would be to examine her for obstruction of the upper respiratory passages, as mouth breathing is a fairly common cause of inflammation of the anterior gingivae in children. Again, since she is in the transition age between deciduous and permanent dentitions, the bleeding may be associated with eruption of teeth.

CHRONIC PROSTATITIS

To the Editor:—One frequently runs into cases of chronic prostatitis, nonspecific, in men past 50 years. Their prostate gland may show a moderate amount of enlargement on palpation. On massage the secretion is loaded with pus cells and a motile bacillus. In the past the only treatment used with these cases was weekly prostatic massage plus occasional passing of a sound. This seldom seems to clear them up. Is there any recent new treatment for these obstinate cases?

Eugene C. Lowe, M.D., Miami, Fla.

ANSWER.—A varying degree of nonspecific chronic prostatitis is common in men over 50 years of age. In the majority of cases the infection is of minor degree and causes few if any symptoms. It rarely becomes acute. However, when the prostatic secretion is found to be loaded with pus cells, it can cause local symptoms and can act as a focus of infection. Prostatic infection may be secondary to other foci, such as tonsils or teeth, and, in persistent cases, these should be excluded. Before treatment is instituted, urographic and cystoscopic studies should be made to exclude the presence of complications, such as prostatic calculi, calculus or tumor in the bladder. Vigorous prostatic massage, carried on daily or every other day for a period of several weeks, usually will reduce the degree of infection to a great extent. Infection in some of these cases may be controlled by various drugs and by antibiotics. Although sulfonamide drugs do not usually eliminate chronic prostatic infection, cases have been reported in which there has been material benefit. Many urologists have reported cases in which the infection was much reduced or eliminated by means of streptomycin or penicillin when employed in large doses. In the presence of coli organisms, streptomycin with alkalinization should be tried first, followed by penicillin, plus acidification. However, all methods of treatment may fail completely, as they have in the case under discussion. As a rule the infection subsides gradually with development of the patient's resistance, and, in the absence of symptoms, it can be largely disregarded.

SYPHILIS IN THE FATHER

To the Editor:—Will you advise me what antisyphilitic treatment is most likely to secure a healthy child in the following case: The husband, 31, denies infection, but admits having a positive Wassermann reaction for six years. He has had almost continuous treatment with oxophenarsine hydrochloride and bismuth compound for four years. Tests show no reduction in titer. The spinal fluid was normal on two examinations. The wife, 27, is pregnant two weeks. She has had negative reactions to three blood tests in the past year.

M.D., Pennsylvania.

ANSWER.—Even though her husband may have syphilis there is no likelihood that a seronegative woman who has never herself been shown to have the disease will give birth to a syphilitic infant. Antepartum infection of the fetus occurs uniformly via the placenta from spirochetemia in the mother. If the father is responsible for the infection of the fetus, it is through first transmitting syphilis to the mother and her transmitting it in turn to the unborn child. Infection of the fetus with syphilis for all practical purposes does not occur in the absence of maternal disease.

In the present instance the father has had his disease for at least six years, and his treatment has been apparently adequate according to accepted standards. Infectious mucocutaneous relapsing lesions are most prone to occur in the first two years of the disease and are uncommon after four to five years even in the absence of specific treatment. Failure of serologic response in spite of the active and prolonged treatment described is in favor of an infection of long standing. Semen is not infectious in the absence of open lesions of the genital tract. An amount of treatment such as is described would make infectious relapse most improbable, unless one is concerned with chronic relapsing disease, of which there is no indication from the history. The likelihood of transmission of infection to the mother from the father at this time is accordingly remote.

It is unusual to obtain a repeatedly negative blood serologic reaction for syphilis in a reliable laboratory in the presence of untreated syphilitic infection, particularly if the disease is active and recently acquired. On the basis of the information given, one would be forced to conclude that the mother is not infected with syphilis. The mother should be observed once monthly during the pregnancy. She should have a repetition of the blood serologic test for syphilis preferably at each of these visits, but as a minimum in the eighth month of the pregnancy and at the time of delivery. If maternal syphilis is diagnosed treatment with penicillin will give satisfactory results at almost any time in the pregnancy and should be commenced immediately, as described in the section on "The Prevention of Prenatal Syphilis" in the special article by the Syphilis Study Section of the National Institute of Health on the "Status of Penicillin in the Treatment of Syphilis" (J. A. M. A. **136**:877 [March 27] 1948).

Provided the mother remains seronegative for syphilis throughout the pregnancy, no special study of the newborn infant for the disease is necessary. As a final precaution a blood test should be taken on the infant at the age of four to six months, which if negative for syphilis will satisfactorily and completely rule out the possibility of congenital syphilis.

THYMUS GLAND

To the Editor:—In this small town we take care of our newborn babies, using pediatricians in cases requiring help. Of the 2 babies that were autopsied the cause of death was said to have been an enlarged thymus gland. Because of this, I have been routinely making roentgenograms of all infant thymus glands with the surprising result of finding more than one-half of these slightly to greatly enlarged. These infants were referred to roentgenologists for radiation treatment and discharged following a negative roentgenogram.

In Boston roentgenograms were made of the thymus in all children as part of their pretonsillar examination, and those who presented enlargement were not operated on. 1. Are we being slack in not having roentgenograms made of the thymus before tonsillectomy? 2. Am I placing too much importance on the problem?

M.D., Massachusetts.

ANSWER.—The dimensions of the thymus as shown by roentgen examination do not present conclusive evidence that an enlarged gland threatens the life or health of the infant. The thymus is rarely, if ever, sufficiently large to cause pressure on the trachea or the bronchial tree thus causing suffocation; infrequently an abscess or an infiltrating neoplasm might cause pressure on the adjacent organs. The thymus does not produce a hormone, nor is it a gland of internal secretion. The former conception of the status thymicolymphaticus has not been proved, and this condition is no longer accepted as a valid explanation of sudden death in infants or as a constitutional state.

In answering the questions propounded it may be stated briefly: 1. An enlarged thymus gland as shown on the roentgenogram is no longer regarded as an evidence of disease or a threat of sudden death. 2. Surgeons and pediatricians no longer require roentgenograms of the thorax to determine the size of the thymus before performing tonsillectomy.

Long years of investigation have failed to reveal the function of the thymus; its function being unknown, it is obvious that the dysfunction is equally obscure. Continued research may some day clear up the unsolved problem of the thymus gland.

GASTRIC MOTILITY AND ALTITUDE

To the Editor:—What is your opinion regarding a small residue of barium in the stomach six hours after a routine series of roentgenograms of the upper part of the gastrointestinal tract, without demonstrable lesions? Please furnish references on correlation of gastric motility and six hour retention of barium in high altitudes.

Captain, M.C.

ANSWER.—In the absence of any roentgenologically demonstrable duodenal or pyloric stenosis, or any other gastroduodenal lesion, the presence of a small amount of barium in the stomach after six hours is probably not of clinical significance. Fluoroscopic study of gastric peristalsis and ability to empty would be of interest in evaluation, as would a test meal with examination of gastric aspirate after five to seven hours.

A delay in gastric emptying in high altitudes has been reported and attributed to anoxemia of the tissues. It is questionable, however, whether this is merely transitory and attributable to a reflex inhibition of gastric motility secondary to the giddiness and other symptoms commonly experienced in sudden exposure to high altitudes.

Reference:

Nimeh, W.: Emptying of the Normal Stomach in Altitudes, Rev. Gastroenterol. **14**: 763-775, 1947.

BROMHIDROSIS

To the Editor:—Could you give me any information on the value of roentgen treatment in bromhidrosis? A patient has been afflicted with this condition for years. Have you any other suggestions as to therapy?

L. C. Gerlinger, M.D., Fostoria, Ohio.

ANSWER.—The query does not state whether the bromhidrosis is general or local. The treatment is similar to that for hyperhidrosis. Roentgen therapy is useful in many cases of local forms. Great care should be used lest excessive doses be employed that lead to untoward results. If moderate amounts of radiation are unsuccessful, it is wise to discontinue and try other methods. Excessive dryness and roentgen burns are worse than the original trouble. The use of chemicals, such as 1 to 10 per cent formaldehyde in alcohol, boric acid solu-

tion or powder, sodium bicarbonate 5 per cent in talcum, potassium permanganate, 1 per cent, as a paint, or as wet dressings, 1 to 1,000, is helpful. Aluminum chloride, 25 per cent, is the basis of many commercial preparations. For extreme degrees of hyperhidrosis and bromhidrosis of hands and feet, sympathectomy has been suggested. Iontophoresis is said to be effective temporarily. The patient may be excreting sweat of offensive odor after ingesting drugs such as valerian and asafetida, or foods like onion or garlic. Poor states of general health and emotional upsets may be a background to hyperhidrosis and bromhidrosis.

MALE STERILITY

To the Editor:—What is the newest form of treatment for a man with sperm count of 10,000,000 with 85 per cent motility, 50 per cent at the end of five hours, 85 per cent abnormal forms of all kinds. The wife is normal in every way. I have built up his general health; other physical abnormalities were not noted. He has received anterior pituitary lobe hormone by injection—100 units weekly for twelve weeks.

M.D., New York.

ANSWER.—More than one specimen of semen should be examined before it is concluded that the foregoing picture represents the patient's average production. If such proves to be the case, a testicular biopsy is indicated. If this shows hypoplasia, degeneration or atrophy of the seminiferous tubules, as is only too probable with semen as poor as the specimen described, then little benefit can be expected from any sort of treatment. If, on the other hand, the germinal epithelium proves to be in fairly good condition, further attempts may be made to stimulate it. The effect of gonadotropic therapy is uncertain and unpredictable, but it sometimes happens that one type succeeds where others fail. Hence equine and chorionic gonadotropins might be tried in the present case. In general, fertility is favored if a patient's basal metabolic rate is maintained at the plus 10 level. Carefully regulated administration of thyroid may be used as needed to accomplish this purpose.

OCULAR HEMORRHAGE

To the Editor:—Please furnish advice regarding treatment of a patient who is 65 years of age, arteriosclerotic, and is myopic—16 D.—in both eyes. He had a choroidal hemorrhage in the macular region of his left eye two months ago with resulting loss of central vision. Vision in his right eye is poor because of corneal opacities following corneal ulcers in childhood. What will (*a*) prevent any further hemorrhages and (*b*) improve his vision? O. M. Haarburger, M.D., Cape Town, Africa.

ANSWER.—(*a*) Rupture of the lamina vitrea in an elderly arteriosclerotic person with high myopia is not rare. The prognosis and treatment of this condition when complicated by macular choroidal hemorrhage is hopeless. He can be assured, however, that he will not become entirely blind, but will likely always be able to find his way about. Treatment with rutin, tocopherol and/or iodides (sodium or potassium) by mouth can be tried. Rest, both local and general, is advisable, and strenuous physical exertion must be avoided. If the arteriosclerosis is accompanied by vascular hypertension, this is particularly important. (*b*) Telescopic lenses may be tried, but the restricted field of view often is worse than the affliction. Full correction of the refractive error is advisable. The patient should be instructed to use his peripheral vision to the full capacity. Simple training along this line is often helpful. Corneal transplant of his left eye might be considered. The vision in this eye, however, might well be permanently affected as the result of nonuse over so long a period.

MALNUTRITION

To the Editor:—How does one go about putting weight on a person? My patient is a young woman of 27, married and has a child age 2. She is 5 feet, 1 inch (155 cm.) tall and weighs 95 pounds (43.1 Kg.). She seems normal in every way; viz., basal metabolic ratio, menstruation, chest, blood (hemoglobin, 78 per cent), development. Her appetite is only fair. I have tried high caloric diet and insulin, but instead of gaining she has lost 2 pounds (0.9 Kg.). I have been tempted to try testosterone propionate, since Dr. Fuller Albright suggested that it is the anabolic hormone. Would it do her any harm? If not, what dosage should I use?

M.D., Canada.

ANSWER.—The treatment of malnutrition is difficult. Whereas testosterone propionate will promote anabolism of many tissues, it should not be used on an essentially normal person such as the patient in question, because of the tendency to virilism. Furthermore, one can build up tissue only to a limited degree with this agent when one is dealing with an essentially normal patient.

HEMATURIA

To the Editor:—In a man aged 26 years hematuria was discovered for the first time during a routine urinanalysis March 1945. Renal function tests, clotting tests, intravenous pyelogram, intramuscular and intravenous dye injection, roentgenogram of the kidney and genitourinary tract failed to determine the source of bleeding. In July 1946 cystoscopy disclosed normal bladder, ureteral ostia, trigonum and vesical neck; catheters passed readily to both renal pelves; the urine returned clear with normal drip from the right side, slightly bloody from the left. Plain roentgenograms revealed no evidence of stone, and a left retrograde pyelogram revealed a perfectly normal kidney, pelvis and major and minor calices. Hematuria continued without pain or fever. Guinea pig tests in August 1945 and August 1946 were negative; in September 1945 tonsillectomy gave no improvement. From December 1945 to June 1946 cystoscopy and all other tests were repeated. In August 1946 cystoscopy and other tests were repeated with negative results. Hematuria continues in changing amount without interruption up to the present. Please give suggestions concerning diagnosis and treatment.

M.D., New Hampshire.

ANSWER.—In view of the duration of hematuria and the lack of other symptoms and signs, it is possible that the bleeding originates from one or more varices on the renal papillae or from a small angioma. The latter would be a more likely diagnosis, especially if hemangiomas are present elsewhere over the body. Repetition of the retrograde pyelogram may reveal slight fuzziness of the calices, which would speak for varices. The instillation of 1 or 2 per cent silver nitrate into the renal pelvis might be tried as a means of controlling the bleeding. If hemorrhages are severe enough to cause anemia or other disturbance, a nephrectomy is indicated.

THYROIDECTOMY IN AURICULAR FIBRILLATION

To the Editor:—Should surgery of the thyroid be contemplated in a woman aged 55 with an exophthalmic goiter and a basal metabolic rate of plus 38? She has an auricular fibrillation.

L. Edward Giovine, M.D., Woodside, N. Y.

ANSWER.—The presence of auricular fibrillation is not a contraindication to a subtotal thyroidectomy for exophthalmic goiter in a woman 55 years of age. The patient should be properly prepared for operation and the basal metabolism reduced to normal with the administration of propylthiouracil supplemented for one week preceding the operation with the administration of iodine. The risk of a thyroidectomy in a patient with heart disease is little greater than in a patient without heart disease, provided that adequate preoperative preparation is carried out.

CARBON DISULFIDE

To the Editor:—A young man, shortly after going to work in a rayon plant where he states that he is exposed to acetone fumes, developed a rather obscure illness consisting of arthralgias and slight fever. Laboratory work, electrocardiograms and appropriate roentgenograms all failed to reveal abnormality. The illness subsided spontaneously, and the patient returned to work. After forty-eight hours, the symptoms returned and again subsided on rest. Can you give me any information as to any toxic reactions to acetone or to the products used in rayon manufacture? Would there be any possible connection between this patient's exposure and his illness?

M.D., Pennsylvania.

ANSWER.—Acetone, of all industrial solvents, is one of the least toxic. In attempts to fix tolerable limits 3,000 parts per million of acetone in air have been rejected as too stringent by one group devoted to standard provisions. This may be contrasted with the standard for carbon disulfide, which unofficially is 10 parts per million. Should this patient be employed in the manufacture of viscose rayon, the possibility of exposure to highly dangerous carbon disulfide should be explored. This substance provides the outstanding danger in that chemical process. Manifestations are legion, but the absence of the normal corneal reflex is the most suggestive single indication of chronic carbon disulfide involvement. Adequate discussions of the action of carbon disulfide may be found in: Johnstone, R. T.: "Occupational Medicine and Industrial Hygiene," St. Louis, C. V. Mosby Company, 1948, and Gordy, S. T., and Trumper, M.: Carbon Disulphide Poisoning, *Indust Med.* **9**:231, 1940.

TELEVISION SCREENS

To the Editor:—Is there harmful effect produced by the television screen? If so, how can this be minimized? Alfred Lilienfield, M.D., New York.

ANSWER.—It is believed that harmful radiation from the household television screen does not occur. Some experimental television screens may emit harmful radiation. This is not certain and it is being studied.